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DIABETES AMONG NATAL INDIANS

BY

J. E. COSNETT, M.B., Ch.B., B.Sc., M.R.C.P.

King Edward VIII Hospital, Durban

Peculiarities in the nature of the diabetic syndrome in tropical countries have long been recognized. In 1907 a symposium on this subject was organized by the Section of Tropical Medicine of the British Medical Association (*B.M.J.*, 1907). The speakers described their experience of diabetes in India and North Africa and made some observations which are of interest in the light of modern knowledge. Several contributors stressed its prevalence among the Hindu races and outlined the strange epidemiological distribution in India. Observations were made on the rarity of "acute cases" in young people, the relatively small number of cases in which ketosis was detected, the infrequency of coma, and the occurrence of cases of "diabetic coma" without acetone or diacetic acid in the urine.

Since these observations were made the existence of two main types of diabetes among people of European origin has been recognized (Himsworth, 1949 ; Lawrence, 1951). In this paper I refer to the diabetes of young, often underweight people who need insulin to prevent ketosis as "type 1." "Type 2" describes the form of diabetes which occurs characteristically in obese middle-aged patients who can be treated by diet and who are not liable to ketosis, except during infections. Recently further reports have indicated that some diabetics in tropical and subtropical countries do not conform to these types. In 1951 DeZoysa described clinical variations of the diabetic syndrome in Ceylon. He stressed the mildness of the disease, the rarity of ketosis and coma, and the low incidence of juvenile diabetes. Most of his patients were sensitive to insulin. A study of Jamaican diabetics by Hugh-Jones (1955) led him to define a further type of diabetes. These type J diabetics develop the disease before the age of 40 years and are usually underweight. They are insulin-resistant, but do not readily develop ketosis when insulin is withheld.

The present study is concerned with Asians (Indians) living in the subtropical climate of Natal. During an analysis of hospital admissions it was shown that diabetes is an exceptionally common disease in this Indian community. It appears that it is much more frequent in the Indians than among the Bantu population, in whom it is relatively rare (Cosnett, 1957). In view of this finding, and others which indicated that Indian diabetics showed peculiar features, a more detailed analysis of a further series of patients has been made.

Material and Methods

The 207 diabetics in this series were admitted to a medical unit during a period of 15 months. Some selection occurred in that a small proportion of diabetics treated in surgical wards have not been included. The series contains both Hindus and Moslems. The Hindus predominate in approximately the same proportion as they do in the hospital population. Diabetes does not seem more prevalent in either religious group.

Diagnosis was based on history and clinical examination, glycosuria, elevated fasting blood-sugar levels, and in some cases on glucose-tolerance curves. Most of the patients were recently diagnosed diabetics who were admitted to hospital on account of complications. In two cases the diabetes was thought to be the result of chronic pancreatitis. In one the diagnosis had been proved by laparotomy and pancreatic biopsy. The other showed pancreatic calcification on *x*-ray examination. In both there was biochemical evidence of chronic pancreatic insufficiency. In certain other respects these two patients differed from the remaining diabetics in the series. In no other case was the diabetes secondary to recognized specific endocrine disorder.

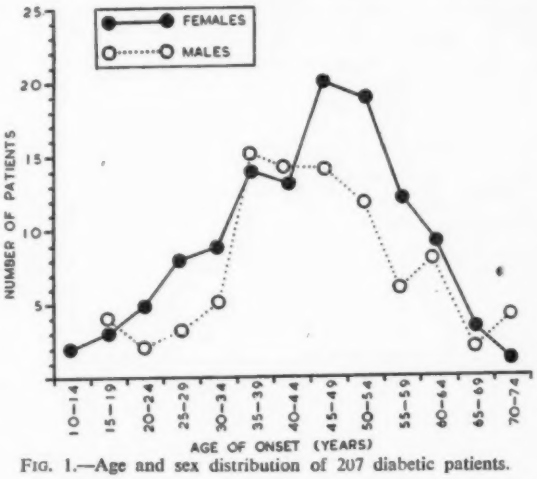

FIG. 1.—Age and sex distribution of 207 diabetic patients.

Age and Sex Incidence.—Of the 207 patients, 118 (57%) were women and 89 (43%) men. The sex and age distribution at diagnosis is shown in Fig. 1. It appears that the maximum susceptibility to diabetes occurs at a slightly earlier age among the Indians than it does among Europeans (Pincus *et al.*, 1934; Himsworth, 1949 ; Pyke, 1956). The same feature was noted in the previous series of Indian diabetics (Cosnett, 1957).

Family History.—A definite family history of diabetes was recorded in 59 cases (28.5%). This corresponds

with findings among European diabetics. No correlation could be found between the type of diabetes and positive family history.

Body Weight

In the absence of any standard weight tables for this race the heights and weights of these patients were compared with the tables of the American Medico-Actuarial Investigation as quoted by Davidson (1954). Certain adjustments were made to allow for the lighter clothing worn by these patients in hospital. In the final analysis all weights were expressed as percentage of standard weight. These data were recorded in respect of 194 patients. The condition of the remaining 13 would not permit accurate measurements to be made.

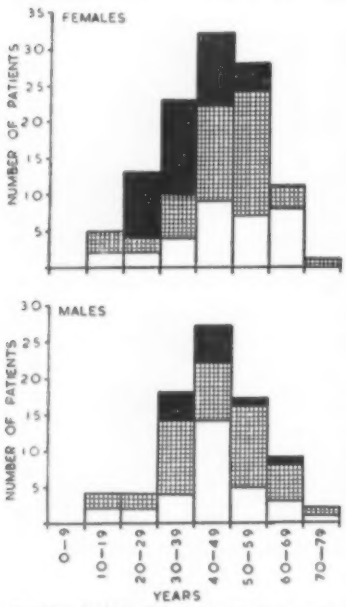

FIG. 2.—Relationship of age to weight. Black areas: Overweight (over 110% standard). Shaded areas: Normal weight (90–110% standard). White areas: Underweight (less than 90% standard).

Fig. 2 shows weight distribution in the various age groups. Patients whose weight was more than 110% of standard are regarded as overweight. Underweight patients are those who weighed less than 90% of standard. The mean weights of patients in the various age groups, expressed as percentage of standard weight, are shown in Fig. 3. The surprising feature is that, while many female diabetics diagnosed in the second, third, and fourth decades are overweight, diabetics diagnosed in later life tend to be of normal or subnormal weight. This is in contrast with experience of European patients, in whom one expects a considerable proportion of obese diabetics among those diagnosed after middle age (Pyke and Please, 1957). Tulloch *et al.* (1956) have described a similar peculiarity among Jamaican diabetics. Many of their patients over the age of 40 were underweight, though in other respects they could be classified as type 2. It might be argued that, where medical control is inadequate, thinness is a factor which allows diabetics to survive past middle age. It is unlikely that this is the whole explanation. Among Natal Indians deaths are not sufficient to explain the rarity of overweight patients after middle age.

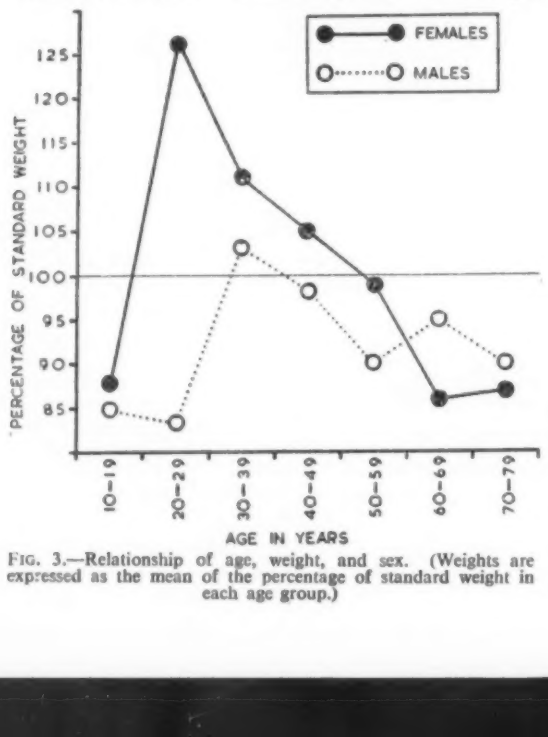

FIG. 3.—Relationship of age, weight, and sex. (Weights are expressed as the mean of the percentage of standard weight in each age group.)

Treatment and Insulin Requirements

Local circumstances add certain difficulties to the treatment of diabetes in this community. Most of the patients attending hospital are from the middle- and lower-income groups. Many of them, especially those of middle age and beyond, are both illiterate and indigent. They can neither afford nor fully comprehend the dietary regulation which is necessary for control of their illness. Their diet is often predominantly carbohydrate, and restriction either imposes severe hardship or is impossible. There is a prevalent belief that diabetes is curable. Freedom from symptoms is often interpreted as cure. Other patients put their faith in a variety of indigenous herbs. Choice of the herbs is usually based on the assumption that a bitter medicine will cure a surfeit of sweetness.

Treatment with insulin is likewise difficult in such a community. Long distances, illiteracy, and a natural reluctance of these patients to give their own injections make many of them dependent on friends and relations who are ill-qualified to give insulin. This leads to irregular and inconsistent treatment. The relative absence of obesity among these patients, especially the older ones, contributes towards difficulty in management. One is reluctant to restrict the diet of a patient who is already below standard weight. In some cases this course has been adopted in an effort to keep the insulin dose reasonably low. After starting treatment with insulin it has been found that many patients are relatively resistant to it. The use of large doses of long-acting insulins by out-patients under these conditions leaves the prescriber's mind somewhat uneasy.

Twenty-nine of the patients in this series were controlled by diet alone. In the absence of a dietetic service at this hospital we have employed a standard diet containing approximately 1,300 calories a day (carbohydrate 100 g., protein 65 g., fat 70 g.) and composed of foodstuffs available to the majority of these patients. The calorie value is supplemented by allowing greater amounts of bread or rice as the situation demands. The stringency of the diet is determined by the degree of obesity, and sometimes by the degree of insulin resistance encountered. Twelve patients were adequately controlled by means of an oral hypoglycaemic agent (tolbutamide). In six cases, for various reasons, control was never achieved.

Table I shows the requirements of 189 patients who were treated with insulin and diet. A feature of diabetes in this race is insulin resistance at all ages. According

to Stocks (1949) the majority of diabetics in England and Wales require less than 50 units a day. Most of these Indians required more than this amount. Insulin resistance is also reflected in the rarity of hypoglycaemic reactions, both in hospital and among out-patients. This feature is fortunate, for the use of large doses of long-acting insulins in these circumstances might otherwise be

TABLE I.—*Daily Insulin Requirements in* 189 *Patients*

No. of Units	No. of Patients	%
0 (controlled on diet) ..	29	15·3
1–49	58	30·6
50–99	76	40·2
100–149	19	10·1
150–199	4	2·1
200 and over	3	1·6

hazardous. Every effort was made to achieve control by a single daily injection. Experience has shown that co-operation is best when treatment is simplest. Insulin zinc suspension (I.Z.S.) was the type of insulin used in the ultimate control of almost all these cases.

The most severe hypoglycaemic reactions encountered were in the two patients whose diabetes was the result of chronic pancreatitis, and in one man who developed Addison's disease, with marked reduction of insulin requirements. These cases stand out in contrast to the others by virtue of their insulin sensitivity.

Ketosis

A striking but providential feature is the surprising rarity of ketosis in a population in which diabetes is not only exceptionally common but is so often diagnosed late and treated inadequately. Indeed, the infrequency of ketosis may be partly responsible for the diagnostic delay, especially in young diabetics. The care-free attitude to treatment may in some cases result from the absence of alarming complications until it is too late.

The lack of ketosis prevails at all ages. In this series of patients there were only two cases of severe ketosis unassociated with infection or trauma. There were several thin young diabetics, requiring large doses of insulin to control glycosuria, who never developed ketosis even when insulin was discontinued. These cases fulfil the criteria of type J diabetes. The following case exemplifies this type.

An unmarried 16-year-old girl who was estimated to be 7% below standard weight was admitted to hospital for control of diabetes which had been discovered during an attack of boils. The fasting blood sugar was 255 mg. per 100 ml. and the glucose-tolerance test produced a rise of 170 mg. per 100 ml. one hour after a dose of 50 g. of glucose. The urine gave a persistent brick-red reaction to Benedict's test. On admission a trace of acetone was present in the urine, but this disappeared rapidly. After considerable difficulty, moderate control was achieved on a diet of approximately 1,500 calories and a dose of 200 units of I.Z.S. daily. The patient was allowed home. She was not seen again for seven months, when she returned to hospital complaining of headache and giddiness. She admitted having had no insulin for three months. There was again brick-red glycosuria, a fasting blood sugar of 310 mg. per 100 ml., but no acetone in the urine. The diabetes was again moderately well controlled on a dose of 210 units of I.Z.S. daily.

In this case as in many others, dietary regulation and large doses of insulin were required to make any impression on the diabetic state.

Other Complications

The nature and frequency of the common complications encountered are shown in Table II. Those patients classified as hypertensive had a systolic blood pressure over 180 mm. Hg or a diastolic pressure over 100 mm. Hg. The 35 cases of peripheral neuritis were all patients who had both symptoms and signs of this condition. Milder cases, in which absent ankle-jerks were the only abnormal finding, were not included. There is a striking absence of any cases of cholecystitis or cholelithiasis. The rarity of gall-bladder disease in this race has been recorded previously (Cosnett, 1957).

Infections of various kinds were the commonest complications, but the gravest were those which belong to the broad group of vascular disorders. This group includes those conditions which manifest as hypertension, retinopathy, albuminuria, peripheral vascular disease, and, in some cases, peripheral neuritis.

The clinical syndrome which is associated with Kimmelstiel–Wilson disease of the kidneys is now well recognized (Gilliland, 1951). Among the Natal Indians

TABLE II.—*Complications Encountered Among* 207 *Patients*

Complication	Type and Criteria	No. of Patients	Percentage (of 207)
Ketosis	Severe with no infection ..	2	1·0
	,, ,, infection ..	4	1·9
	Mild ,, no infection ..	3	1·4
	,, ,, infection ..	13	6·3
Infections	Cutaneous and subcutaneous ..	43	20·8
	Urinary	24	11·6
	Pneumonia; lung abscess ..	7	3·4
	Pulmonary tuberculosis ..	12	5·8
	Other	8	3·9
Vascular	Hypertension (over 180/100) ..	63	30·4
	Peripheral vascular disease: gangrene, claudication or absent pulses	19	9·2
	Retinopathy	55	26·6
	Albuminuria: without urinary infection	32	15·5
	Cerebral vascular accident: thrombosis or haemorrhage ..	12	5·8
	Coronary thrombosis	3	1·4
Neural	Peripheral neuritis: with symptoms and signs	35	16·9
	Cranial nerve affection	3	1·4
	Visceral neuropathy	1	0·5
Cataracts	All types	24	11·6

the condition appears to be exceptionally common. In this series the diagnosis could be made with some confidence in 24 cases (11%). The main criterion for the diagnosis was the coexistence of gross albuminuria, hypertension, and diabetic retinopathy in a patient in whom these features could not be otherwise explained. Most of these patients were oedematous, some were in cardiac failure, others showed evidence of impaired renal function, and nine of these patients had peripheral neuritis. Renal biopsies were not performed and necropsies were not permitted in the three patients who died of the condition. No definite correlation could be found between body weight and liability to development of this syndrome.

Several other cases were observed in which the complete syndrome was not yet fully developed. Through these cases it has been possible to obtain a composite picture of the natural history of the disease, until its usual termination in renal failure and uraemia. It is possible that this final uraemic coma in a diabetic may explain the "diabetic coma without ketosis" which was described during the 1907 symposium.

A further significant observation was the amelioration of the diabetic state which occurred in these patients

as the renal disease progressed. The value of this series is limited by the short period these patients were under observation, but the data available support the conclusions of Zubrod *et al.* (1951) concerning this phenomenon. These workers showed that patients with Kimmelstiel–Wilson disease of the kidneys often required less insulin, had lower fasting blood-sugar levels, and showed less tendency to ketosis in the later stages of the disease. Diabetics with normal kidneys, or with other types of renal disease, did not behave in this manner. In our patients we have encountered definite reduction of insulin requirements and decrease in glycosuria and blood-sugar levels in advanced cases of the Kimmelstiel–Wilson syndrome.

In two cases, not included in this series because of insufficient proof, the retrospective diagnosis of diabetes was made on the grounds of uraemia, hypertension, oedema, gross albuminuria, and retinal changes resembling those of diabetes. Both patients gave a history of diabetes which had been "cured." Neither had glycosuria or elevation of blood-sugar levels when they were admitted to hospital. Both died of renal failure with uraemia, but permission for necropsy was not obtainable.

In the light of modern knowledge of this syndrome it is interesting to review the remarks made at the 1907 symposium on diabetes in the tropics. Among these are to be found such statements as: "Albumen is to be found in most chronic cases. . . ." "It is frequently noted that sugar diminishes with increase of albumen in the urine." "Albuminuria . . . is the most frequent complication of diabetes." "The quantity of albumen has generally been found to vary inversely as that of sugar. When albumen continues to be excreted in large amounts with traces or even absence of sugar in the urine, we know for certain that the poor patient has not many days to live. All the symptoms of chronic albuminuria begin to appear: puffiness of the face, oedema of the whole body and of the lungs, dilatation of the heart, all come in rapid succession; the patient complains of breathlessness and suffers badly from dyspnoea, and coma generally ends the scene." "The appearance of albumen depends more on the chronicity of the disease than the amount of sugar passed in the urine. The nature of the kidney change in such cases is more like chronic interstitial nephritis . . . causing sclerotic changes in the arteries."

These observations, made in India over 50 years ago, correspond with present experience of Indians in Natal. The following case history illustrates many of these features of diabetes.

A 47-year-old man was admitted to hospital three times in one year. His mother, two maternal uncles, and an aunt all suffered from diabetes. The patient had been diabetic for six years, but apparently never adequately treated. On the first occasion, when he was admitted for control of diabetes, he was estimated to be 7% below standard weight for his height and age. The fasting blood sugar was 400 mg. per 100 ml. There was no acetone in the urine, but there was profuse albuminuria with a few hyaline casts. His blood pressure was 170/105 mm. Hg. Advanced diabetic retinopathy was present and there were signs of peripheral neuritis. The diabetes was eventually controlled on a dose of 220 units daily, with a diet of approximately 1,400 calories. Nine months later he was admitted to hospital with oedema of the legs. He was 4 lb. (1.8 kg.) heavier than on the previous admission. The fasting blood sugar was 360 mg. per 100 ml. The urinary findings and blood pressure were unchanged. Serum albumin was 1.7 g.% and globulin 2.3 g.%. The blood urea fell from 72 mg. per 100 ml. on admission to 40 mg. after 10 days. On this occasion it was possible to control the diabetes with the same diet and a dose of 60 units of I.Z.S. daily. The oedema was relieved by mercurial diuretics. Six weeks later he was again admitted to hospital with left ventricular failure and generalized oedema. When a glucose-tolerance test was done the fasting level was 135 mg. per 100 ml., and this rose to a maximum of 295 mg. two hours after a dose of 50 g. of glucose. There was intermittent slight glycosuria (yellow-green to Benedict's test), but this was easily controlled on his previous diet. He did not require insulin. An electrocardiogram showed changes compatible with hypertensive heart disease. The blood urea was initially 64 mg. per 100 ml., but this fell to 29 mg. The heart failure and oedema were responding to treatment, when, on the eighth day of his third admission, he developed precordial pain and died within a few minutes. Death was presumed to be due to coronary thrombosis.

This case illustrates the amelioration of the diabetic state that occurs in advanced cases of the Kimmelstiel–Wilson syndrome. It is unfortunate that sentiment and religious prejudice prevented necropsy proof of the diagnosis in such cases.

Parity and Prediabetes

Pyke (1956) showed that the preponderance of female diabetics could be explained partly on the grounds of parity, although parity does not lead to the earlier appearance of diabetes. Among the Natal Indians early child-bearing and large families are common. The parity of the 110 married diabetic women in this series is shown in Table III. The proportion of diabetics of both sexes in this community is approximately the same as that found among Europeans. It is thus unlikely that this high degree of parity is playing any part in the prevalence of diabetes among the Indians.

TABLE III.—*Parity of* 110 *Married Diabetic Women*

Parity	0	1–3	4–6	7–9	10–12	Over 12
No. of women ..	4	22	25	30	19	10

All the mothers in this series were questioned regarding the size of their babies at birth. Fourteen were able to state that one or more of their offspring had weighed more than 9 lb. (4 kg.). The heaviest recorded baby was one of 14 lb. (6.4 kg.). A further 10 patients did not know the birth weights of their babies but stated that one or more of them had been "very big." In addition there were 12 women who had one or more stillbirths but did not give a definite history of big babies. From this evidence it is likely that the phenomenon of prediabetes occurs in association with the variety of diabetes prevalent among Natal Indians. The only significant correlation which could be discovered was one with obesity. Of these 36 patients, 19 were estimated to be overweight (more than 110% standard weight) and 7 were underweight. No definite correlation was found with family history, insulin requirements, or liability to complications.

Clinical Varieties of Diabetes

In presenting his analysis of Jamaican diabetics Hugh-Jones (1955) used a scatter diagram which related age of onset to insulin requirements and showed the presence of ketosis and degree of obesity. The same procedure has been adopted with this series of Indian diabetics. Fig. 4 shows the distribution of 193 patients.

Thirteen patients have been omitted because their condition would not permit measurement of height and weight.

There are nine cases which undoubtedly possess the criteria for classification as type J diabetics. These are patients less than 40 years of age who required 100 units or more a day to control the diabetes. None of these was ketotic or overweight. A further nine cases, four of them overweight, required between 80 and 100 units daily, and are also considered to be of this type. The incidence of type J diabetes in this series is therefore 8.7%, which is slightly more than that found by Hugh-Jones in Jamaican diabetics.

With regard to the remaining cases, several striking features emerge. There is a singular absence of juvenile diabetics who are prone to ketosis and sensitive to insulin (type 1). There are only two patients who approach this type, and both have atypical features. One was a 17-year-old boy whose weight was 10% below standard when he was admitted to hospital for control of diabetes. This was achieved on a dose of 100 units of I.Z.S. daily. Shortly afterwards he defaulted, ceased taking insulin, and was readmitted in diabetic coma. There was no evidence of infection at the time. He was again subsequently controlled by 100 units of I.Z.S. daily. The other patient was a 13-year-old girl who had previously been in another hospital with diabetic coma and boils. She was controlled on 60 units of I.Z.S. daily, but a few months later she was admitted to this hospital on account of persistent glycosuria. On this occasion there was transient ketosis. Her insulin requirement had increased to 110 units daily, but there was no further infection. The high insulin requirements of these two cases are unusual for recently diagnosed type 1 diabetics.

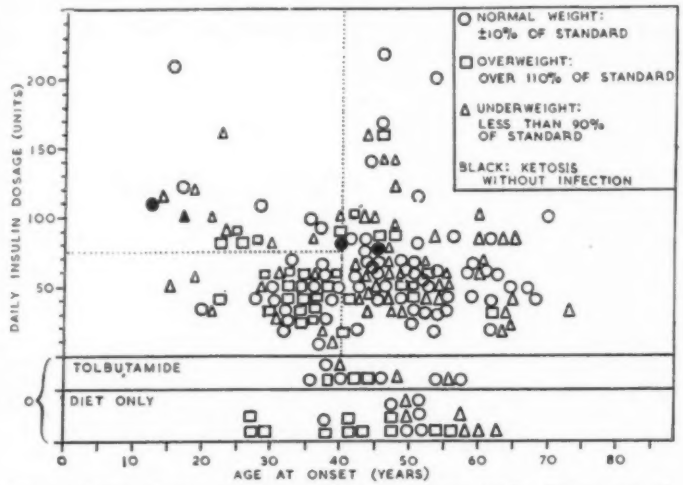

FIG. 4.—Scatter diagram showing relationship between insulin dosage, age of onset and body weight in 193 patients. Cases of ketosis not associated with infection are shown in black.

There is a further distinct group of young diabetics, between the ages of 20 and 40 years, who require less than 75 units daily, but these cannot be regarded as belonging to type 1. They were all free of ketosis and most of them were overweight women (Fig. 2). But for their earlier age of onset, they resemble type 2 diabetics.

Beyond the age of 40 years there is wide variation both in insulin requirements and in body weight. Relatively few of these patients could be controlled by diet alone. The most striking peculiarity of these middle-aged and elderly diabetics is the absence of obesity among them. Few of them are overweight (Figs. 2 and 3).

Discussion

The significance of these geographical variations in the clinical picture of diabetes is not known. Their occurrence serves to emphasize the belief that diabetes is not a single disease but a symptom-complex of varying aetiology. The value of studying these variants of diabetes lies in establishing relationships between them, and in determining the presence of common factors in aetiology, clinical picture, and complications. Clinical impressions may then serve as a guide to endocrinologists and biochemists in the further elucidation of cause and effect.

The main impression gained from this study of Indian diabetics has been one of a form of diabetes which is exceptionally common, free from ketosis, and resistant to insulin. Analysis has shown a relative rarity of type 1 diabetes, the occurrence of type J diabetes, and a large residue of diabetics who may be classified as type 2, but who are unusual by virtue of age distribution and body-weight behaviour.

From their clinical features and behaviour it can be assumed that these Indian diabetics do not lack endogenous insulin. Lawrence (1951) has suggested that the obese, insulin-resistant middle-aged diabetic (type 2) has fat stores which are replete and unable to accommodate further sugar. Any excess therefore becomes apparent in the blood and urine. It is possible to explain the existence of thin insulin-resistant diabetics on the same basis if we presume that fat storage is controlled by a threshold mechanism. Owing to a hormonal or enzymic disturbance the threshold is raised, transfer of glucose to fat depots is restricted, and this leads to the appearance of diabetes before the patient can become obese. The extreme degree of this restriction of fat deposition is represented by the rare diabetic who has no fat stores and who is extremely resistant to insulin (Lawrence, 1951).

Consideration of the possible causes of this metabolic disturbance involves speculation on the effects of heredity and environment. At first sight it appears that the peculiar variations of diabetes among Natal Indians are due alone to racial predisposition. That this may not be so is suggested by the strange distribution of diabetes in India, being prevalent in some areas and rare in others. Furthermore, there is evidence that many cases of diabetes in India may be classified in the orthodox manner into the two types prevalent among Europeans. About 12% of patients reported by Singh (1957) were liable to ketosis on withdrawal of insulin. His patients showed a tendency to be obese rather than underweight. In Bombay the hospital admission

rate of diabetics appears to be about one-sixth of that prevailing among Indians in Durban, yet 24 of 289 diabetics were in diabetic coma when they were admitted to hospital (Director, Indian Council of Medical Research, 1956, personal communication). Freedom from ketosis is therefore not peculiar to the whole Indian race. In Ceylon, however, ketosis is rare (DeZoysa, 1951).

If an environmental factor is to be incriminated we are fortunate in being able to compare the incidence and nature of diabetes among the three racial groups in Natal: Bantu, Indian, and European. Among the latter diabetes resembles that of white races elsewhere. In the Bantu diabetes is relatively uncommon, but severe ketosis is not unusual. These facts allow one to exclude climatic conditions and certain dietary factors. The basic dietary constituents among the poorer of both non-European races are similar. Malnutrition occurs in both races. In the search for an environmental factor which is peculiar to Indians the most obvious finding is the large variety of herbs consumed as food or flavouring, or occasionally for therapeutic purposes. At least six species of indigenous herbs are eaten by almost all Indians, but not by the Europeans or the Bantu in any quantity.

The striking similarity between diabetes in Jamaica and that of Natal Indians leads one to look for common environmental factors in these two races. The two communities are as widely separated ethnologically as they are geographically. Hugh-Jones (1955) comments on the variety of herbs which are used by Jamaicans as bush teas, and mentions the possibility of these causing diabetes. Is it possible that among these herbs is one, or more, common to certain areas of India, Ceylon, Jamaica, and Natal that interferes with carbohydrate and fat metabolism to produce a diabetic syndrome? Alternatively, a dietary factor may modify diabetes in such a way that it becomes insulin-resistant and not apt to produce ketosis. This reasoning may be facile, and it leaves other aspects unexplained. It does, however, show the need for more detailed clinical, epidemiological, and botanical study in these countries.

Summary

Diabetes mellitus is exceptionally common among Natal Indians. In the course of an analysis of 207 diabetics in hospital the disease has been found to show certain peculiarities, some of which have been described in other tropical and subtropical countries. The diabetes of young people which is associated with liability to ketosis and sensitivity to insulin (type 1) is very uncommon. Instead there occurs a form of juvenile diabetes which is characterized by insulin resistance and freedom from ketosis (type J). Between 20 and 40 years of age there is a group of overweight diabetics, mostly women, who are more sensitive to insulin. Beyond the age of 40 years insulin requirements vary, but patients are more often underweight than overweight. Ketosis is rare among Natal Indians, but infections and vascular complications of diabetes are common.

In several respects there is a resemblance between the types of diabetes occurring among Natal Indians and those described in Jamaica. These findings are discussed in relation to peculiar forms of diabetes reported in other tropical countries.

I thank Dr. N. A. Rossiter, under whose care these patients were admitted to hospital; Professor E. B. Adams and Dr. G. D. Campbell for helpful criticism; and Dr. S. Disler, medical superintendent, for permission to publish this report. I am grateful to the Director, Indian Council of Medical Research, for information regarding diabetes in India.

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CARBON MONOXIDE HAZARD IN ANTARCTICA

BY

L. G. C. E. PUGH, M.A., B.M., B.Ch.

National Institute for Medical Research, London

Carbon monoxide poisoning is an important hazard in polar exploration. Amundsen, Byrd, and Stefansson have each described narrow escapes from fatal asphyxiation by CO, and Stefansson (1940) focused attention on the subject in his book *Unsolved Mysteries of the Arctic*. Henderson and McCullough Turner (1940) described experiments with the Nansen cooker showing that under certain conditions dangerous amounts of CO might be given off.

The Nansen stove introduced by Fridtjof Nansen in 1890, and used by Shackleton and Scott on their Antarctic expeditions, had a "primus" stove as its heating unit and was popular with explorers because of its lightness and high thermal efficiency. This amounted to 80–90% (Henderson and McCullough Turner, 1940), compared with 40–50% for a primus stove used with an ordinary cooking-pot (unpublished data). Unfortunately Henderson and McCullough Turner found that when the Nansen stove was used for melting snow or ice CO was produced in the highly dangerous concentration of 0.08 to 0.1%, and this may be one reason why the Nansen stove is no longer used.

Irving, Scholander, and Edwards (1942) studied the uptake of CO in persons using primus stoves in tents and snow-shelters, and reported blood COHb levels of 15–18% saturation after one to three hours. Among the tents tested, significant absorption of CO occurred only in those constructed of plastic-treated fabric which were more or less airtight.

In Antarctic exploration, where mechanized transport is rapidly replacing dog sledges for long-distance travel, there is the additional risk of CO poisoning from exhaust fumes. The importance of this hazard has been brought to light by the experience of the Commonwealth Trans-Antarctic Expedition. Both the British and the New Zealand parties were affected at times by

symptoms resembling those of CO poisoning during the crossing of the Antarctic plateau. The circumstances are described in this paper, together with some experimental observations carried out by the Anglo-American physiological team at Scott Base (Pugh, 1957). Also presented are the results of experiments carried out in London on the CO output from primus stoves, as used on the Trans-Antarctic Expedition.

CO Poisoning on the Commonwealth Trans-Antarctic Expedition New Zealand Team

The New Zealand party of five men led by Sir Edmund Hillary travelled in modified Ferguson tractors, one of which towed a small caravan or caboose containing the radio equipment. The caboose was heated by a radiator connected to the exhaust pipe of the vehicle ahead, and was equipped with two primus stoves for cooking. The tractor drivers took it in turns to rest and warm up in the caboose while travelling, and the party forgathered in it at halts. Hillary and the radio-operator, P. Mulgrew, slept in it, while the others slept in tents. Primus stoves were kept going in both the tents and the caboose for four to five hours a day. At sea-level all went well, but on the way up the Skelton Glacier symptoms consistent with CO poisoning began to appear and grew worse as the party ascended. The symptoms were most severe at the plateau depot at 8,000 ft. (2,440 m.) during a spell of unusually calm cold weather with temperatures of −35 to −38° F. (−37 to −39° C.). Those who spent much time in the caboose, in particular Hillary and Mulgrew, were affected on and off by the following symptoms, in various combinations: loss of appetite, severe headaches, weakness, shortness of breath on exertion—and occasionally even at rest—and a feeling of constriction in the chest. Mulgrew also complained of attacks of dizziness, buzzing in the ears, and precordial pain. Hillary on one occasion collapsed on leaving the caboose.

At first the symptoms were either disregarded or attributed to altitude; but, when it became obvious that something else was wrong, the air over the primus stoves in the caboose was tested with a CO detector, which gave a weakly positive result (0.005% CO). A small leak in the exhaust heater which had been causing fumes was repaired, and later a draught chimney was fitted up over the primus stoves. After this the symptoms improved, only to return when the chimney was blocked up because of the cold. Hillary and other members of the party, however, stated that they never really became acclimatized to the altitude on their journey to the South Pole, although they were never more than 10,000 ft. (3,050 m.) above sea-level. At the plateau depot Hillary said he felt very much as he had done in the Himalayas on camping for the first time at 16,000 ft. (4,875 m.). He and Mulgrew had occasion to return to Scott Base from the plateau depot, and they found it took them nearly a week to recover their normal health.

The British Crossing Party.—Similar symptoms were noticed by some members of Sir Vivian Fuchs's team after leaving the South Pole station, when the onset of low temperatures caused them to travel with the windows of their vehicles closed. There was one acute episode which will be described elsewhere by the expedition's medical officer, Dr. Allan Rogers. After this accident they took care to keep the windows of their vehicles open, and had no further trouble.

The British Advance Party (1956–7).—The following account of symptoms on the Trans-Antarctic Expedition advance party has been given by Dr. Rainer Goldsmith (personal communication).

In the crate in which the T.A.E. advance party spent the winter at Vahsel Bay, ventilation was rudimentary. The size of the crate was 20 ft. by 7 ft. 6 in. by 3 ft. (6 by 2.3 by 0.9 m.). It served as mess, kitchen, and recreation room, and for all other functions which required shelter for their performance. The drift snow after a few months reached roof level. Cooking was done on three primus stoves, and on a number of occasions the atmosphere was so foul that matches would not remain alight nor the stoves burn with a blue flame. Symptoms of CO poisoning were not uncommon. Men suffered from violent frontal and vertical headaches, relieved after a night in the tent, and on two occasions nausea and vomiting were experienced. The symptoms usually followed a prolonged stay in the crate.

Experimental Studies

Blood CO Levels

Samples of venous blood for CO determination were taken from members of Sir Vivian Fuchs's party at the South Pole and at Scott Base. Blood CO levels were also determined on members of a sledging team who had been in the field for four months, and on other personnel at Scott Base who were non-smokers. The analyses were performed by the special method for small quantities of COHb described by Scholander and Roughton (1943). Haematocrit values were also determined. The blood samples taken at the South Pole were obtained almost seven hours after the party arrived

TABLE I.—*Blood CO Contents (Vols. % STPD) and Percentage Hb Saturation (Figures in Parentheses) in Members of the British Trans-Antarctic Party, New Zealand Dog-sledge Teams, and Others at Scott Base*

Smokers	Non-smokers; or No Smoking for 24 Hours*
British Trans-Antarctic Party	
J.S.: 0·37 (1·5) South Pole	H. Le G.*: 0·92 (3·4) Scott Base
H.L.: 0·55 (2·3) " "	R.H.*: 1·27 (5·5) " "
D.S.: 1·02 (4·3) " "	G.P.: 0·67 (3·9) " "
A.R.: 0·55 (2·3) " "	K.B.: 0·90 (3·7) " "
V.E.: 0·57 (2·3) Scott Base	
J.S.: 0·70 (2·8) " "	
New Zealand Dog-sledge Teams	
G.M.: 0·38 (1·8)	R.B.*: 0·15 (0·7)
	B.G.: 0·17 (0·8)
	R.M.: 0·10 (0·4)
Others at Scott Base	
B.D.: 0·64 (3·0) Before tractor driving	E.P.H.: 0·12 (0·6)
0·90 (4·2) After 40 min. tractor driving	F.C.: 0·15 (0·7)
	G.M.: 0·15 (0·7)
	A.P.: 0·13 (0·6)

there; those taken at Scott Base were obtained within an hour of arrival. None of the men concerned were actually suffering from symptoms at the time of taking blood.

The results (Table I) did not show any evidence of undue accumulation of CO; the blood levels in the crossing Antarctic party were comparable to the values found in smokers in London, which in this laboratory vary from 0.3 to 1.3 vols. %. However, on comparing members of the crossing party, who either did not smoke at all or who had not smoked that day, with non-smoking base personnel, it is seen that the CO levels in the former range from 0.67 to 1.27 vols. %, compared with 0.12 to 0.15 vols. % in the latter. Evidently, therefore, the crossing party were absorbing CO from some external source apart from smoking. Their experience after leaving the South Pole—when they had

symptoms consistent with CO poisoning which cleared up after attending to the ventilation of their vehicles, as well as the low CO levels observed in the dog-sledging team, who, like the crossing party, slept in tents—suggest that absorption of CO was taking place in the vehicles and not in the tents. The COHb levels before and after tractor-driving are of interest in that the subject had been driving an open tractor with a vertical exhaust pipe opening at head level. They show that a measurable rise in blood CO can occur even in a vehicle without a cabin if the exhaust pipe is so placed that fumes can be blown in the direction of the driver's face.

Absorption of CO in Tents

No opportunity presented itself of investigating the uptake of CO in the Trans-Antarctic parties' Sno-cats, but blood CO levels were investigated in one of the expedition's tents on a subject using a primus stove (*a*) for heating purposes alone, and (*b*) for melting snow. The experiments were performed on two successive days under comparable weather conditions, the outside temperature being 27° F. (−3° C.) and the wind velocity 3–5 m.p.h. The tent was a double-walled pyramid tent of rather heavy cotton fabric with a separate ground sheet, the inside volume being approximately 2.5 cubic metres. The sleeve entrance was kept closed, but the ventilating tube at the apex was left open to simulate ordinary conditions of use.

In the first experiment the stove burnt continuously for over three hours. In the second it went out several times after two hours, and the experiment was discontinued. In this experiment the subject melted snow in an open container, pouring away the water and starting afresh as the container filled with water.

The results (Fig. 1) show a progressive increase in blood CO which was more than twice as rapid when the stove was used for melting snow as it was when used for heating alone; but in neither experiment was a dangerous level reached, and the subject experienced no ill effect apart from the heat. In a subsequent experiment in London, in which the CO concentration inside a light-weight single-walled pyramid tent, set up in a laboratory, was followed over three hours while ice was being melted over a primus stove, the CO content did not rise above 0.003 vol. %, which corresponds to a blood COHb level of less than 5% saturation. This tent was constructed of a light-weight nylon–cotton fabric ("wincol") as used on the 1953 Mount Everest expedition. The results indicate that with such a tent dangerous accumulation of CO is unlikely to occur, even in still air, owing to diffusion of air through the fabric.

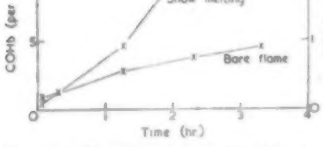

FIG. 1.—Blood carbon monoxide in a subject using a primus stove in an Antarctic tent.

Output of CO from Primus Stoves

A lighted primus stove was placed in an upright metal drum of approximately 100-litre capacity. The opening at the top was closed with a well-fitting lid provided with a central outlet pipe. Air was admitted at the bottom by an inlet pipe. In the initial experiments the combustion gases were simply aspirated into a Tissot spirometer by suction at a measured rate of approximately 100 l./min. The spirometer was filled and emptied twice before gas samples were taken. With this arrangement it was found that the flame went out in two to three minutes whenever a container full of ice was placed on the stove. In order to improve the air supply a pump was attached to the inlet pipe and air was forced in at a rate of 300 l./min.: the combustion gases were pumped into a large Douglas bag via a dry gas meter.

The gases collected in the spirometer or in the Douglas bag were analysed for O_2, CO_2, and CO. O_2 and CO_2 were measured on a Scholander gas analyser; CO was determined on an infra-red apparatus after removal of water-vapour and CO_2. Separate experiments were carried out with two well-used primus stoves. The stoves were pumped up until a maximum flame was obtained, but, apart from this, no attempt was made to secure a constant size or colour of flame. The stoves were used (*a*) alone, and (*b*) with a cooking-vessel filled with ice chips. The effect of air–nitrogen mixtures was also studied; but under these conditions results could be obtained only with the bare flame, because the flame went out too quickly when the cooking-vessel was placed on the stove.

When the primus stoves were used without the cooking-vessel the concentration of CO in the aspirated gas mixture varied from 0.002 to 0.005 vol. %, and the volume of CO produced per minute varied from 2 to 5 ml. The oxygen consumption was 2.2 to 3.7 l./min. with a CO_2/O_2 ratio of 0.53 to 0.63. The volume of CO per litre of O_2 consumed was 0.7 to 2.2 ml. With O_2-deficient gas mixtures, it was found that the flame went out when the O_2 content of the combustion gases fell to 13–14%. With the O_2 below 17% the CO concentration rose to 0.01–0.015%.

When the cooking-vessel full of ice chips was placed on the stove the concentration of CO rose to 0.023–0.060%, and the CO output rose to 50–70 ml./min. or 10.2–26.8 ml./l. O_2. It was found that the stove would burn only as long as the aspirated gas contained 18% O_2 or over; and just before the flame was extinguished the CO concentration sometimes rose as high as 0.165%. The production of CO was not appreciably reduced by allowing the ice to melt and bringing the water to near boiling-point, but was prevented by interposing an asbestos mat between the flame and the cooking-vessel.

The results of these experiments are in general agreement with those obtained by Henderson and McCullough Turner (1940) with the Nansen cooker. These workers also found that the evolution of CO from a primus stove burning freely under good conditions of air supply was negligible, but that dangerous amounts of CO were given off when cooking-vessels filled with ice were used, especially when the air supply was restricted.

Discussion

Absorption and Physiological Effect of CO

The rate of absorption of CO at various concentrations of CO in the air breathed and the permissible concentrations of CO in the blood are shown in Fig. 2 (Forbes, Sargent, and Roughton, 1945; Henderson *et al.*, 1921; Drinker, 1938).

In experimental studies in which the desired blood level of COHb is reached rapidly and maintained only

for a short period of time, partial saturations up to 20–30% are tolerated without symptoms by healthy adults during rest or moderate physical exertion (Haldane and Priestley, 1935; Asmussen and Chiodi, 1941; Apthorp *et al.*, 1958); but, as Haldane emphasized, such exposures may be followed by tiresome headaches coming on some hours later. At saturations between 40 and 50% there is impairment of mental function and ataxia, and collapse may occur on exertion. Few investigators have exposed themselves to levels above 50%. Haldane once reached 56% saturation, at which level he was completely incapacitated and in imminent danger of collapse.

In experiments designed to study the effects of long exposures to low concentrations of CO, Sayers, Merewether, and Yant (1922) found that the symptoms of CO poisoning developed at lower blood concentrations and were more severe at any given blood concentration than in short experiments. These investigators reported tightness across the forehead or slight headache at COHb saturations of 16–20%, which were reached in six hours of breathing 0.02% (2 parts in 10,000 of air). COHb saturations of 22–28% were associated with moderate to severe headache, with or without dizziness and nausea. In a later investigation, however, three out of six subjects remained free of symptoms at these COHb levels even after six hours' exposure (Sayers *et al.*, 1929).

In life situations, where a given blood level is reached slowly or is maintained for a long period of time, the first symptom is usually headache, followed by dizziness

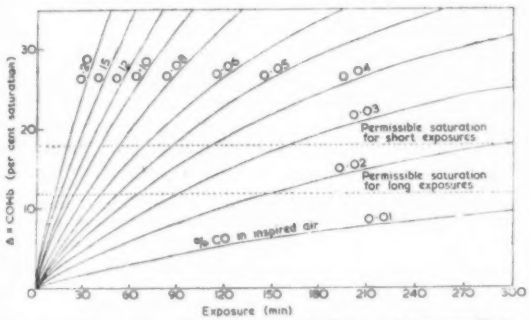

FIG. 2.—Absorption of CO by man in light activity (ventilation 9.5 l./min.) (after Forbes *et al.*, 1945).

and nausea, and a tendency to collapse on exertion. With rapid poisoning, the victims may become paralysed before they realize that anything is wrong. In cases of fatal poisoning blood COHb levels of 60–80% saturation are the rule, but fatalities have occurred at much lower levels. In a series of 68 fatal cases reported by Gettler (1943), 25% had less than 60% of COHb, and 4.5% of cases had levels between 30 and 40% saturation.

CO and Altitude

When persons at high altitude are exposed to low concentrations of CO symptoms are experienced at much lower blood concentrations and the effects are more severe. In aviation the assumption has been that, for practical purposes, the effect of a given blood level of COHb is the same as that of an equivalent degree of arterial O_2 unsaturation due to reduced barometric pressure (Heim, 1939; Armstrong, 1952). Experimental justification for this assumption has been provided by visual sensitivity tests (McFarland, 1946). On this basis, an altitude of 10,000 ft. (3,050 m.), which reduces the arterial O_2 saturation to about 85% (Luft, 1956), is equivalent to a COHb saturation of 97−85=12%; and 12% COHb at 10,000 ft. (3,050 m.) is equivalent to a height corresponding to an arterial O_2 saturation of 85−12=73%, or 16,000 ft. (4,875 m.). Altitude has no significant effect on the rate of CO absorption in man (Forbes, Sargent, and Roughton, 1945; Lilienthal and Pine, 1946), but it does influence the final concentration reached in the blood after many hours of exposure, because of the change in the partition of Hb between CO and O_2 at low O_2 tension (Table II).

TABLE II.—*COHb Content of Blood as Percentage Hb Saturation, in the Presence of Various Partial Pressures of CO at Sea-level and at 10,000 ft. (3,050 m.), Calculated from a Standard O_2 Dissociation Curve by the Method of Roughton and Darling (1944), Assuming the Arterial pO_2 at 10,000 ft. to be 63 mm. Hg and the Relative Affinity of CO for Hb to be 238 Times that of O_2 (Joels and Pugh, 1958)*

CO% (Dry Gas at Sea Level)	pCO mm. Hg	COHb	
		Percentage Sea-level	Saturation 10,000 ft. (3,050 m.)
0·005	0·04	8·5	11·6
0·010	0·25	15·6	20·7
0·020	1·50	27·0	35·2
0·030	2·25	36·1	46·2
0·040	3·00	44·8	52·4

CO from Primus Stoves

Reference to Fig. 2 shows that the concentration of CO produced by the naked flame of a primus stove is negligible so far as symptoms are concerned: the concentrations observed during cooking or snow-melting would be unlikely to cause symptoms in under an hour; and even the high concentrations just before the stove went out would be tolerated for half an hour. However, the O_2 consumption and rate of CO production is such that in a confined space, like Hillary's caboose or the advance party's crate, a considerable deficiency of O_2 and accumulation of CO would gradually develop in the absence of ventilation with fresh air.

The blood concentrations of COHb observed in tents by Irving *et al.* (1942) and by ourselves at Scott Base were not sufficient to cause symptoms at sea-level, although they would do so at 10,000 ft. (3,050 m.). Irving and his associates used tents made of impervious material in their experiments, pointing out that, although tents are not normally made of impervious fabric, diffusion of air through the wall of a tent in cold weather may be practically abolished by accumulation of snow and ice, and the condensation of moisture on the inside. That such a condition may in practice be realized is shown by the fact that, just as in the T.A.E. advance party's crate, the air in a tent may become so vitiated that the primus stove goes out and it becomes difficult to light a match. Instances of this are given by Irving *et al.* (1942), and the same thing has been described to me by Sir Vivian Fuchs and other members of his party. Irving and his colleagues did not melt ice in their experiments, and had they done so their COHb figures would no doubt have been higher.

Fortunately, explorers are protected from CO poisoning in such circumstances by two factors: (1) the time spent in melting snow and preparing food is always kept to a minimum—usually about half an hour; and (2) during the dangerous period when a cooking-vessel is being used the stove tends to go out at a relatively high oxygen concentration—namely, 17–18% compared

with 13–14% with the stove used for heating alone. This happened in the second experiment at Scott Base, causing the experiment to be given up after two instead of three hours when the subject's blood COHb, though beginning to rise steeply, was still at a comparatively safe level of 15%.

CO and the T.A.E.

Although confirmation by blood gas analysis was not obtained, there can be little doubt that both parties on the Antarctic plateau suffered at times from the effects of CO, or more correctly a combination of CO and altitude, for their story suggests that they might have escaped symptoms altogether had they been travelling at sea-level. The advance party kept three primus stoves going in a small crate with practically no ventilation, so it is not surprising that they should have had symptoms, even though they were at sea-level.

In Sir Vivian Fuchs's party the important factors were the long periods of travelling, which amounted to 10–16 hours a day, and the onset of extra cold weather which caused them to keep the windows of their vehicles closed. Since exhaust gas contains anything between 3% and 10% CO (Sayers and Davenport, 1937; Fitton, 1956) even a small leakage of fumes from the engine compartment into the cabin could be dangerous if inhaled over many hours. The New Zealand party were likely to have been exposed over shorter periods to higher concentrations of CO, since two primus stoves were used simultaneously for cooking and heating in a small caravan which lacked the safeguard of air-permeable walls.

The symptoms complained of by the parties on the plateau were a mixture of those characteristic of altitude and those of CO intoxication. Headache is, of course, an early symptom in both conditions: dizziness, precordial pain, and tinnitus are more typical of CO poisoning (Drinker, 1938). Hyperpnoea, anorexia, lassitude, and weakness are the characteristic effects of altitude as experienced on Himalayan expeditions, where the ascent is roughly comparable to that of Hillary's party on the Skelton Glacier. Altitude symptoms are not, however, encountered below 12,000 ft. (3,660 m.) in the Himalayas and are usually not severe below heights of 14,000–18,000 ft. (4,265–5,485 m.): even then they tend to pass off in a few days (Pugh and Ward, 1956).

According to Hillary the symptoms were very much like those he had experienced on first going to 16,000 ft. (4,875 m.), although the actual height was only 8,000 ft. (2,440 m.). This statement can be used as a basis for calculating the probable COHb content of his blood. The alveolar O_2 tension for a person living at 8,000 ft. (2,440 m.) who ascends rapidly to 16,000 ft. (4,875 m.) would be about 42 mm. Hg (Rahn and Otis, 1949). Subtracting 2 mm. Hg for the alveolar-arterial O_2 gradient at such an altitude gives an arterial O_2 tension of 42 mm. Hg, the corresponding O_2 Hb saturation being 75% (Luft, 1956). Since the arterial O_2 saturation for an acclimatized person at 8,000 ft. (2,440 m.) is about 90% the equivalent COHb would be only about 15% saturation, which at sea-level would be unlikely to cause symptoms.

Summary

Carbon monoxide poisoning on the Commonwealth Trans-Antarctic Expedition is described. The symptoms occurred mainly at 7,000–10,000 ft. (2,135–3,050 m.) and represented a combination of the characteristic effects of altitude and CO. In the British party symptoms were associated with long hours of travelling in motorized vehicles with the cabin windows closed. In the New Zealand party symptoms were associated with shorter exposures in a small caravan provided with an exhaust heater and two primus stoves for cooking.

Symptoms of CO poisoning were also experienced by the T.A.E. advance party who spent the winter of 1956–7 in a crate, with three primus stoves for cooking and heating purposes.

The output of CO from primus stoves was investigated, and the absorption of CO was studied in a subject using a primus stove in an Antarctic pyramid tent.

The physiological effects of breathing low concentrations of CO at sea-level and at altitude are discussed.

I wish to thank the members of the Trans-Antarctic Expedition for their collaboration in this work.

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The executive board of W.H.O. began its 23rd session at Geneva on January 20 under the chairmanship of Dr. P. E. MOORE, director of Indian and Northern Health Services of Canada. The session is expected to last two or three weeks, and during it the board will review W.H.O.'s programme for 1960. The 18 members of the board, which is a technical non-political body, are health experts designated to act on behalf of the World Health Assembly. The present board is composed of members designated by the following countries: Afghanistan, Australia, Brazil, Canada, France, Guatemala, the Federal Republic of Germany, India, Iran, Italy, Liberia, Mexico, Tunisia, United Arab Republic, United Kingdom, United States of America, U.S.S.R., and Viet Nam.

SLEEP AND WAKEFULNESS AT HIGH ALTITUDES

BY

E. S. WILLIAMS, M.B., B.S., B.Sc.

Registrar in Radiotherapy Department, Middlesex Hospital, London: lately House-Physician, Chester City Hospital

During the British North Greenland Expedition of 1952–4 studies were made (Lewis and Masterton, 1957) of the sleep pattern of men living as a partially organized community in an environment devoid of the diurnal cycle of light and darkness. It was demonstrated that the average total sleep taken per day was uninfluenced by the polar conditions but that the sleep/wakefulness pattern varied greatly from the usual pattern of the individuals studied. It was also shown that there was a seasonal change in the number of nights of broken sleep but that there was no correlation between the occurrence of such nights and the taking of naps.

The present study aims at demonstrating the effect of high mountaineering on these same characteristics of sleep rhythm. So far as I am aware no investigation of sleep similar to that carried out in North Greenland has previously been attempted during a mountaineering expedition.

Methods

The subjects of the investigation were three men aged 30–33 and a woman aged 26. Each was supplied with record cards identical with those described by Lewis and Masterton (1957), and records were kept for about two months of normal life and during an expedition to the Karakoram Mountains of West Pakistan. On these cards all periods of sleep were marked as a thick line, breaks in sleep appearing as breaks in the line. Naps taken during a waking period appeared as a very short line in an otherwise blank space. A "nap" was a sleep of not longer than three hours (usually much less) and separated from the termination of the main sleep by at least one hour.

Sleep/wakefulness diagrams were prepared following the method adopted by Kleitman and Engelmann (1953). Such a diagram is a rectangle, one side of which represents the number of days in a month normalized to unity (so that months of differing length can be directly compared), the other side representing the 24 hours in a day. The area of the rectangle therefore represents the number of hours in a month. The number of days on which the subject slept during any given hour of the day divided by the number of days in the month is the "sleep fraction" for that hour. This is shown in black in the diagram for each hour of the day, so that the pattern of sleep for the whole month can be seen at a glance.

The records were analysed in two parts: those relating to sleep habits below an arbitrary altitude of 10,000 ft. (3,050 m.), and those made during the time spent between 10,000 and 20,000 ft. (3,050 and 6,100 m.). The time spent above the 10,000 ft. level was in every case continuous, and much the greater part of this time was above 15,000 ft. (4,570 m.).

Results

The average sleep per day taken while living above 10,000 ft. was greater than the average while below this level. This is shown in Table I. The probability of this difference being due to chance is shown in each case in the last column.

TABLE I

Subject	Below 10,000 ft. (3,050 m.)			Above 10,000 ft. (3,050 m.)			Average Excess of Sleep when Above 10,000 ft.	Probability of this Excess Being Due to Chance
	Period in Days	Average Sleep per Day (hours)	Standard Deviation	Period in Days	Average Sleep per Day (hours)	Standard Deviation		
Female	71	6·827	1·615	50	7·784	1·739	0·957	Approx. 0·04
Male 1	72	6·964	1·671	50	7·645	1·619	0·681	Approx. 0·10
,, 2	56	6·873	1·455	60	7·213	2·093	0·340	Approx. 0·45
,, 3	62	7·483	1·338	60	8·488	1·613	1·005	< 0·01

The sleep/wakefulness pattern became more coincident with the diurnal cycle of light and darkness as shown in Figs. 1 and 2.

The number of nights of interrupted sleep was greater above 10,000 ft. than during life in England, but the tendency to experience this showed a marked individual variation (Table II).

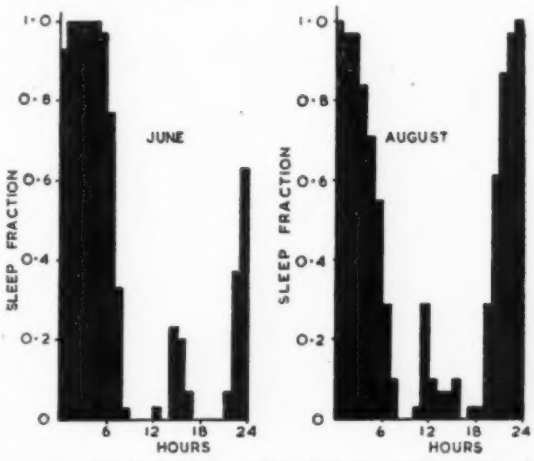

FIG. 1.—Sleep/wakefulness pattern for one month (June) of ordinary life and for one month (August) spent at an altitude above 15,000 ft. (4,570 m.). The blocked areas represent the fraction of the month spent in sleep. This individual was in the habit of taking naps, and the habit persisted at high altitudes.

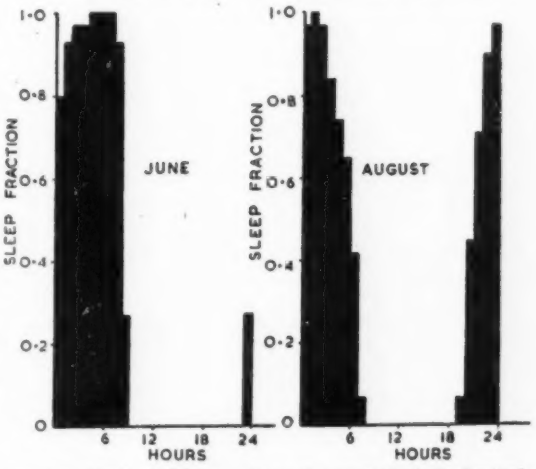

FIG. 2.—Sleep/wakefulness patterns for an individual who took no naps either in ordinary life or in the mountains. Here, and in Fig. 1, is seen the tendency to advance the hour of going to sleep while at high altitudes.

TABLE II

Subject	Percentage of Nights when Sleep was Interrupted		Total Naps	No. of Times Naps Followed Period of Sleep < Average	No. of Times Broken Sleep Followed by Nap or Naps
	Above 10,000 ft.	In England			
Female..	22%	3%	7	7	0
Male 1..	24%	2%	13	10	0
,, 2..	57%	4%	26	19	5
,, 3..	28%	21%	71	36	18

There was no correlation between the incidence of nights of broken sleep and the taking of naps (Table II). The tendency to take naps appeared to be a personal idiosyncrasy, but naps were more often taken during the day following a night when the sleep had been less than the average for the individual concerned.

Discussion

It might be questioned whether the keeping of such a record as that described would itself have an effect upon the sleep pattern. In fact, the observer becomes quite used to noting the time frequently if there is delay in going to sleep, and in noting it immediately on waking. Accuracy to more than a few minutes in recording the onset of sleep is, of course, impossible.

The average sleep per day normally taken showed a wide individual variation. In three subjects the average was less than 7 hours, while in one subject it was almost 7.5 hours. The female member of the party in normal life took no more sleep than the male members.

During the time spent at high levels all four subjects took more sleep per day, but the difference in the mean value above and below 10,000 ft. was significant only in two cases, as seen in Table I. The sleep taken varied greatly from day to day, there being a wide spread of the sleep-frequency diagram (Fig. 3).

The change in the sleep/wakefulness pattern (Figs. 1 and 2) merely reflects the exigencies of mountaineering. The decrease in monthly sleep fraction in the early morning hours is accounted for by the necessity for early morning starts whenever weather conditions permitted. Similarly, the increase in the sleep fraction for the hours before midnight is accounted for partly by the evening drop in temperature driving members of the expedition into their sleeping-bags, and partly as compensation for the usual early start of the working day.

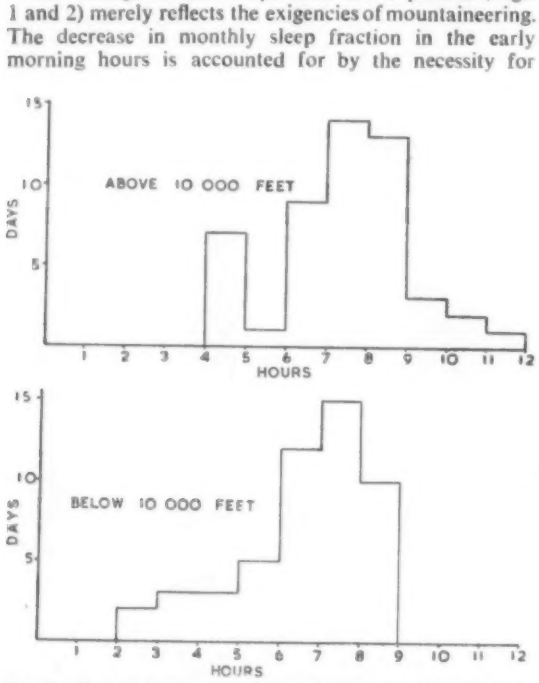

FIG. 3.—Typical frequency diagrams showing the wide spread in the number of hours' sleep taken per day by the same individual during 50 days of normal life and during 50 days at high altitudes.

Interrupted sleep was defined as a night's sleep with more than one break. The percentage of nights on which this occurred for each member of the expedition, compared with the percentage during normal life, is shown in Table II. Individual variations were again large, but there was a general increased tendency to interruption of nights during the time spent at a high altitude. The increase was least when the subject normally experienced frequent nights of interrupted sleep. In one case such interrupted nights were few in normal life but were 57% of all nights spent above 10,000 ft.

It is possible that this increased incidence of interrupted sleep is the factor which has given rise to the belief that climbers at high altitudes sleep less than at low levels. The man who wakes frequently gets the impression that he has slept little. At much higher altitudes than those at which this study was conducted sleep may well be severely curtailed by factors arising from the more marked anoxia, and lower temperatures, encountered.

The lack of correlation between broken sleep and the taking of naps agrees with the findings in the Arctic. The tendency for naps to be taken following a night where the total sleep was below the average for the particular individual confirms common experience, but, on the whole, the taking of naps appeared to be a personal idiosyncrasy.

One subject often took a nap when circumstances permitted, and this habit continued when he was living at high altitudes (Fig. 1). In contrast, another subject rarely took naps in normal life, and neither was it his habit to do so in the mountains (Fig. 2).

Summary

The sleep habits of three men and one woman were studied in normal life and during the time they spent as members of a Himalayan expedition.

The average number of hours' sleep per day while living between 10,000 and 20,000 ft. (3,050 and 6,100 m.) was greater than the average when below this level.

There was a tendency, imposed by the environment, for the diurnal sleep/wakefulness pattern to coincide with the diurnal light/darkness cycle.

The proportion of nights of broken sleep increased at the higher altitudes as compared with the incidence of broken sleep in normal life. The taking of naps was not correlated with broken sleep, but appeared to be an individual idiosyncrasy.

This study formed a part of the scientific work of the London School of Economics Mountaineering Club Himalaya Expedition, 1956, and I gratefully acknowledge the collaboration of the members of the expedition and the financial support the expedition received from the Mount Everest Foundation, from the Medical Research Council, and from the Central Research Fund of the University of London. Thanks are also due to Dr. H. E. Lewis for suggesting the work and for his continued encouragement.

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EFFECT OF ALTITUDE ON BASAL PALMAR SWEATING

BY

PAMELA C. B. MacKINNON, Ph.D., M.B., B.S.
Department of Anatomy, Royal Free Hospital School of Medicine, London

I. L. MacKINNON, M.B., Ch.B.
Department of Anatomy, King's College, London

AND

E. S. WILLIAMS, M.B., B.S., B.Sc.
Middlesex Hospital, London

Kuno (1934) pointed out that the sweat glands on the palmar surface of the hand are primarily occupied in reflecting emotional changes, during which their output may increase or decrease according to the variety and intensity of the emotion. But the factors which are responsible for palmar sweating under basal conditions, when it is assumed that the emotional state is comparatively constant, are unknown.

Variations in basal palmar sweating have been reported in a number of physiological circumstances, and the reports indicate that it diminishes with age (MacKinnon, 1954a), diminishes during the luteal phase of the menstrual cycle (MacKinnon, 1954b), diminishes in pregnancy (MacKinnon and MacKinnon, 1955a), especially during the first and third trimesters (MacKinnon and MacKinnon, 1955b), and diminishes in summer (MacKinnon and MacKinnon, 1956). In each case the authors have felt that the depression in basal sweat output was linked to increased suprarenal activity and that a stress of some sort was responsible.

The present investigation owes its inception to the thesis that the stress of living at high altitudes would be reflected in basal palmar sweating. It was designed to measure the effect of high altitude on basal palmar sweating by comparing sweat indices of four people living for a period of 12 days in the Swiss Alps, and, in the following year, for a period of 40 days in the Karakoram of West Pakistan, with their sweat indices in London.

Methods

Four mountaineers, three men aged 30–33 and a woman aged 26, all normally resident in London, were involved in the investigation.

Sweating was measured by the number of moist spots situated at the openings of the ducts of sweat glands on an area of skin 4 mm. square immediately distal to the central whorl of the right middle finger, after the finger had been dried with blotting-paper. The number is referred to as the sweat index. It was obtained by preparing a plastic fingerprint (Sutarman and Thomson, 1952) on waking in the morning under conditions which were as near to basal as possible and subsequently counting the spots in the selected area of skin at a magnification of 10 (Fig. 1).

In the Swiss Alps records were made for 12 days at altitudes of 6,000–13,000 ft. (1,830–3,960 m.) and compared with those obtained in London during the week before and the week after the expedition. In the Karakoram daily records were made for 40 days at altitudes of 8,000–20,000 ft. (2,440–6,100 m.) and compared with daily records obtained in London for a month before and after. While the plastic fingerprints were being prepared oral body temperature was taken with thermometers which were accurate to 0.1° F. Mean sweat indices and mean body temperatures are given in Tables I and II.

On a few isolated mornings of days when major ascents were to be undertaken sweat prints were not made, and, unfortunately, on the first day in the Karakoram one subject (Male 3) contracted amoebic dysentery, which lasted for four weeks, and his records for the Karakoram are therefore not included.

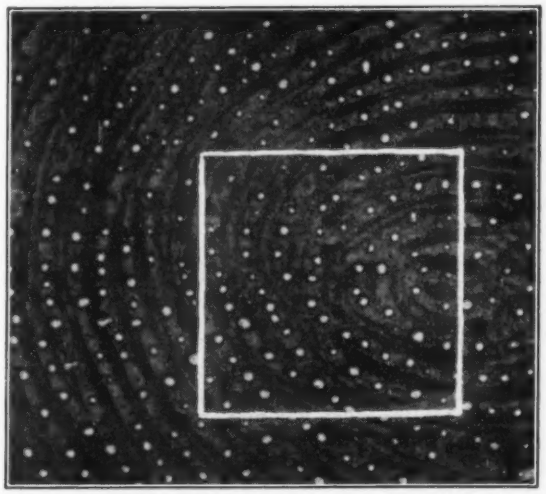

FIG. 1.—Photomicrograph (×10) of a plastic fingerprint with a sweat index of 79. Each white spot represents a moist sweat-duct orifice.

TABLE I.—*Mean Basal Sweat Index and Mean Basal Oral Temperature (°F.) for 12 Days in the Swiss Alps and for 7 Days in London Before (London 1) and After (London 2)*

	London 1. July				Swiss Alps. July				London 2. August			
	Sweat Index	S.D.	Oral Temp.	S.D.	Sweat Index	S.D.	Oral Temp.	S.D.	Sweat Index	S.D.	Oral Temp.	S.D.
Female ..	77	32	97·9	0·6	54	23	97·7	0·8	87	38	98·0	0·4
Male 1 ..	30	19	97·4	0·5	11	9	96·9	0·5	32	17	97·7	0·4
,, 2 ..	45	23	97·3	0·6	12	11	96·8	0·4	82	38	97·3	0·6
,, 3 ..	77	41	97·8	0·4	31	22	96·9	0·6	55	41	97·6	0·5

TABLE II.—*Mean Basal Sweat Index and Mean Basal Oral Temperature (°F.) for 40 Days in the Karakoram and for 30 Days in London Before (London 3) and After (London 4)*

Subject	London 3. April–May					Karakoram. July–August					London 4. October				
	Sweat Index	S.D.	Oral Temp.	S.D.	C1*	Sweat Index	S.D.	Oral Temp.	S.D.	C2*	Sweat Index	S.D.	Oral Temp.	S D.	C3*
Female (follicular)	72	22	98·2	0·4	−2·0840	33	19	98·1	0·6	1·1423	69	14	98·1	0·5	1·0243
,, (luteal) ..	84	10	98·5	0·5	1·4924	30	18	98·2	0·4	−2·4271	—	—	—	—	—
Male 1	39	23	97·3	0·5	0·3148	6	7	97·5	0·6	0·2374	25	28	97·1	0·4	−0·0731
,, 2	57	25	97·6	0·3	−1·0318	30	27	96·9	0·6	−0·9765	64	13	97·4	0·5	0·01193

* Indices of correlation between sweat index and oral temperature in London 3, Karakoram, and London 4 respectively, expressed as the ratios of regression coefficients to standard errors.

Sweat Indices

The mean sweat indices of each of the climbers were lower in the Swiss Alps than in the corresponding London controls (Table I), and lower in the Karakoram than in the corresponding London controls (Table II). From the statistical angle the lowering of the sweat indices in the Swiss Alps was significant and in the Karakoram very strongly significant (Table III).

TABLE III.—*Significance of Differences Between Basal Sweat Indices in Swiss Alps and Karakoram and Those in London Before and After. The Probability That Where a Fall in Body Temperature was Registered in the Alps or Karakoram it Arose by Chance is in Parentheses. All Probabilities were Calculated by t-Testing (Chambers, 1952)*

	London 1		London 2
Female	P<0·05 (P<0·2)	Swiss Alps	P<0·02 (P<0·1)
Male 1	P<0·02 (P<0·01)		P<0·01 (P<0·01)
,, 2	P<0·001 (P<0·05)		P<0·001 (P<0·05)
,, 3	P<0·001 (<P0·001)		P<0·05 (P<0·01)
	London 3		London 4
Female (follicular) ..	P<0·001 (P<0·4)	Karakoram	P<0·001
Female (luteal) ..	P<0·001 (P<0·02)		
Male 1	P<0·001		P<0·001
,, 2	P<0·001 (P<0·001)		P<0·001 (P<0·01)

The day-to-day fluctuations in the sweat indices of the four members of the climbing party followed a similar pattern, and only those of the woman and one man (Male 1) are given (Fig. 2). The graphs illustrate that the characteristic mean sweat index of the individual climbers varied greatly, that the influence of high altitudes on the index was approximately the same in male and female, that the depression in the sweat index was rather less in the Swiss Alps than in the Karakoram, that "acclimatization" did not appear to take place in the Karakoram in spite of the 40 days spent there, and that recovery from the depression in the Swiss Alps appears to have been complete on reaching London 48 hours after leaving the mountains, whereas recovery from the depression of the index by the Karakoram remained incomplete after two months. The last of these did not apply in Male 2, whose sweat indices were slightly higher in London after the Karakoram than in London beforehand (Table II).

Body Temperature

Basal body temperature was lower in the Swiss Alps than in London in all cases (Table I) and lower in the Karakoram than in London in the woman and Male 2, but not in Male 1 (Table II). From the statistical angle the depressions in body temperature were commonly significant (Table III), and it would therefore seem that body temperatures were generally, though not invariably, depressed at high altitudes.

Statistical correlation of sweat indices with body temperature was carried out on three sets of data—those of London 3, those of the Karakoram, and those of London 4—and the low indices which were the result of the investigation (Table II, C1, C2, and C3) provide convincing evidence that on these occasions the sweat indices were not dependants of body temperature. It was therefore assumed that the sweat indices in the Swiss Alps had also been independent of body temperature.

Discussion

During the luteal phase of ovulatory menstrual cycles body temperature is elevated (Tompkins, 1944) and the sweat index is commonly lowered (MacKinnon, 1954b). Therefore, where the observations on the woman were numerous enough—that is, in the Karakoram and in London before and after—follicular data were separated from luteal data. This could not be done for the Swiss Alps because the total period involved, including the London controls, was only 30 days, and luteal data in the Alps were therefore necessarily compared with follicular data in London (Fig. 2). In 1956 this woman's menstrual rhythm was characterized by luteal elevation in body temperature (Table II) without depression of the sweat index (Fig. 2), and if the rhythm of 1955 bore the same characteristics the fall in her sweat index in the Alps, though it took place in the luteum, was attributable solely to altitude, and the fall in body temperature which took place in the Swiss Alps meant that its depression by altitude exceeded its elevation by the luteum.

Conditions which are encountered at high altitudes, and which could be called upon to account for the very significant lowering of the sweat indices in all the members of the expedition, both in the Swiss Alps and in the Karakoram, are low relative humidity, low environmental temperature, low barometric pressure, emotional changes, or perhaps a combination of some or all of these.

Relative humidity in August in the Swiss Alps is 67% (Morikoffer and Chorus, 1941) and in the Karakoram 51% (Bleeker, 1936), while in London the mean relative humidity at 8 a.m. during the months of May to October is 84% (Meteorological Office, 1958, personal communication), and it would therefore seem possible that the lower relative humidity encountered in the Swiss Alps and the Karakoram could have been responsible for a rapid evaporation at the apertures of the sweat ducts, resulting in a low sweat index. But Venables (1955) saw no "evidence of curvilinearity" in scatter diagrams in

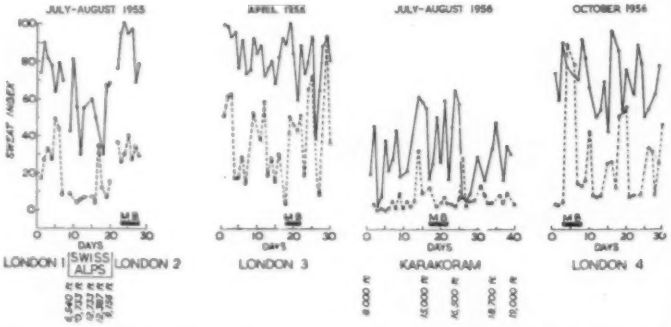

FIG. 2.—Daily indices of basal palmar sweating in female (continuous line) and in male (interrupted line) during expeditions to the Swiss Alps and to the Karakoram, and of daily indices obtained in London before and after the expeditions. M.B. = Bleeding phase in menstrual cycles of female.

which he related relative humidity to psychogalvanic reflexes measured on the palms of the hands of normal subjects, and, as the electrical resistance of the skin by which the psychogalvanic reflexes were measured was equally the measure of sweat-gland activity, it seems doubtful if the reduction of the palmar sweat index in the Swiss Alps and the Karakoram was due to low relative humidity. Also militating against the theory of causation by relative humidity is the fact that the graphite solution used in the preparation of the plastic sweat prints was applied to, and excluded the air from, the finger within five seconds of drying it.

The early morning air temperature in the tents, in both the Swiss Alps and the Karakoram, was around 28–32° F. (−2.2–0° C.), but in spite of this the members of the party felt comfortably warm while the plastic prints were being prepared, because they had been enclosed for six to nine hours in efficient sleeping-bags. Air temperatures encountered later in the day were much higher, and it is true to say that the members of the expedition were only rarely exposed to extreme cold at any time of the day or night. Nevertheless air temperatures in the Swiss Alps and the Karakoram were well below London levels and may have reduced the sweat index in the process of heat conservation, although the primary function of the palmar sweat glands is not thermoregulatory (Kuno, 1934).

Low barometric pressure induces hypoxia, and hypoxia is a potent stimulus to the chemoreceptors in the carotid and aortic bodies in experimental animals (Dripps and Comroe, 1944), thereby giving rise to diverse consequences which include increased activity in the cerebral cortex to a degree that, in dogs, may lead to convulsions (Dripps and Comroe, 1944). If man responds to hypoxia in the same way as experimental animals the hypoxia experienced by the climbers at high altitudes in the Swiss Alps and the Karakoram should have increased their cerebral activity, and, as Netsky and Starr (1948) have demonstrated that precentral corticectomy in man increases palmar sweating as judged by the ferric chloride and tannic acid test (Silverman and Powell, 1944), activation of the precentral cortex by chemoreceptor reflexes induced by anoxia may have contributed to the fall in the sweat index at high altitudes.

Primary emotional changes affect palmar sweating (Kuno, 1934), but it is impossible to judge their influence in the Swiss Alps and the Karakoram. The symptoms —emotional instability, loss of self-reliance, suppressed anxiety, and lack of initiative—usually appear at an altitude of 10,000 ft. (3,050 m.) (Best and Taylor, 1950), or, in the case of experienced mountaineers, at 15,000 ft. (4,570 m.) (McFarland, 1939), but none of these were experienced subjectively by, or seen objectively in, any of the climbers.

Of the factors so far discussed none seems likely to have been the sole cause of the fall in the palmar sweat index in the Swiss Alps and the Karakoram, but a combination of them might constitute a stress (Selye, 1950) involving defensive reactions on the part of the pituitary and suprarenal glands with consequent increase in the blood levels of adrenocorticotrophic and corticoid endocrines, and, as the administration of corticotrophin brings about a fall in the sweat index (MacKinnon, 1957), the fall which took place at high altitudes may have been caused by stress.

Summary

Daily measurements of basal palmar sweating in four people living for a period of 12 days at altitudes of 6,000 to 13,000 ft. (1,830–3,960 m.) in the Swiss Alps, and, in the following year, for a period of 40 days in the Karakoram of West Pakistan were recorded and compared with corresponding data for London. Sweating was found to be significantly less in the Alps and in the Karakoram than in London in all cases. Possible reasons are discussed.

These observations formed a part of the scientific work of the London School of Economics Mountaineering Club Himalaya Expedition, 1956, and we gratefully acknowledge the collaboration of the members of the expedition and the financial support the expedition received from the Mount Everest Foundation, the Medical Research Council, and the Central Research Fund of the University of London. Thanks are due to Mr. J. Durbin, of the London School of Economics, for his advice on the statistical analyses.

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On January 15 Dr. DETLEV W. BRONK, president of the Rockefeller Institute, and Mr. J. R. B. BRETT-SMITH, of the Oxford University Press, New York, announced the establishment of the Rockefeller Institute Press. This will publish books on science and related subjects. Editorial responsibility for the books will rest primarily with the Institute, while the Oxford University Press will be chiefly responsible for design, printing, and distribution. It is expected that the first books will be issued in the autumn of 1959. While many of the books and monographs will be the work of Institute faculty members, works by other scholars will also be published. "Among the objectives of the Press," said Dr. Bronk, "will be to provide an additional and needed outlet for scientific books of highest quality, carefully selected because of their excellence. Further, during this time of rapidly increasing scientific knowledge paralleled by ever mounting costs of publication, the Rockefeller Institute Press, because of its non-profit nature, will make possible the publication of books at costs which will enable the individual to purchase them for his personal library."

THE PROBLEM OF UNILATERAL AMBLYOPIA

A PRELIMINARY STUDY OF 10,000 NATIONAL HEALTH PATIENTS

BY

ROBERT B. WELLESLEY COLE, M.S., F.R.C.S.
Ophthalmic Surgeon, Nottingham

It is not generally known that a substantial proportion of otherwise normal healthy individuals are wholly or partially blind in one eye. This condition of unilateral amblyopia is fairly common. Colloquially known as "lazy eye," it is in reality a serious permanent disability, arising from a failure or breakdown of binocular vision in early childhood. The affected eye is to all intents and purposes otherwise normal. There is no sign of disease in it, and yet it has a low or negligible visual acuity, whereas its partner has normal vision.

The more serious degrees of this type of amblyopia occur in the earliest years of infancy, for at that age the eyes are less developed. In the worst cases central fixation is lost or absent—that is, vision in the affected eye is less than 6/60, and when the other eye is covered the blind eye is unable to fix an object.

The younger the child the shorter the interval required for the weak eye to become permanently blind if neglected. Thus in a child 6 months old permanent blindness (loss of fixation) from neglected amblyopia occurs in six weeks; in a child 12 months old it occurs in six months; in a child of 3 years it takes 12 months to occur. In children of 5 and over permanent loss of central fixation never occurs (Worth, 1903, 1921).

A number of surveys on Service recruits were conducted during the last war. All of these revealed a high proportion of healthy young adults with one useless or amblyopic eye. As a result many authorities on both sides of the Atlantic, including Fulford Eales (1920; quoted by Dorothy Campbell, 1947), Downing (1945), and Dorothy Campbell (1947), have recommended *early routine pre-school examination of all children* to prevent this serious developmental tragedy. Duke-Elder (1949, p. 4012) suggests that such routine examination should take place at the age of one year.

Experience shows that even after apparent cure amblyopia may recur at any time up to the age of 7. So that not only should routine examination of all children's eyes be done as early as possible, but the examination should be repeated regularly until they start school.

Definition of Amblyopia

An eye is regarded as amblyopic if its visual acuity is less than 6/12, in the absence of any pathology. The amblyopia is unilateral if the other eye has normal vision and is two Snellen lines better than the amblyopic eye. Examples of unilateral amblyopia are: 6/12 part or worse (amblyopic eye) and 6/6 or 6/5 (normal eye); 6/18 or worse (amblyopic) and 6/9 or better (normal); 6/24 or less (amblyopic) and 6/12 or better (normal).

In unilateral amblyopia monocular vision replaces binocular vision. There is either a general inhibition of the retinal field (Feldman and Taylor, 1942) or macular inhibition (Travers, 1938), or there is evidence of a scotoma which is "facultative" (Chavasse, 1939) or "absolute" (Evans, 1929) or "relative" (Peter, 1932). A hysterical element has been suggested by some authorities.

The anatomical findings are equally inconclusive. It is known that only the appreciation of form is affected, and not that of colour or of light (Wald and Burian, 1944). But while Pugh (1954) places the anatomical site of the disability at the fovea, King and Passmore (1955) place it in the rods and cones, Clark (1941) in the lateral geniculate body, and Guibor (1944), Burian (1954), and Burian and Watson (1952) in the cerebrum.

Effects

Most sufferers from amblyopia are unaware of it, until by chance one day injury, a foreign body, disease of the good eye, or a routine examination exposes the weakness of the other eye. But such a sufferer is always handicapped. In the worst cases disease or injury of the good eye causes registrable blindness. But, apart from this, the affected eye is always functionally suppressed, and subconsciously the patient uses only his good eye—that is, he is virtually monocular.

Judgment of depth, as in sports and other activities which depend on the stereoscopic value of binocular vision, is handicapped. In motoring, objects approaching from the amblyopic side tend not to be seen until they come within the visual field of the good eye. In America, on the advice of the Ophthalmic Section of the American Medical Association, certain categories of heavy goods drivers have to undergo special tests to exclude amblyopia (*J. Amer. med. Ass.*, 1940).

Examination Under the National Health Service

Under the National Health Service any man, woman, or child can present himself to an ophthalmic surgeon or sight-testing optician for a sight test, with a view to having glasses prescribed, if necessary. Such an examination is free. Most of these patients are healthy, and not unduly worried about their eyes. If they do, they usually go to a hospital out-patient department, where treatment is equally free. In practice most of the patients who seek a sight test under the Supplementary Ophthalmic Service of the National Health Service complain of eyestrain, headache, blurred vision, or other symptoms which suggest that their eyes have difficulty in coping with the demands of their work, school, or enjoyment, such as televiewing or reading the evening newspaper.

The examination required by the regulations is basically one of refraction. But before refracting each patient it has always been my practice to examine the eyes *clinically* so as to exclude any pathological condition, and so assess the *functional coefficient* of the eyes.

Any untoward findings are communicated to the patient's doctor, without whose co-operation much of the value of the examination would be lost. For example, since many of the family doctors have become aware of the prevalence of amblyopia the number of very young children of amblyopic parents who have been sent to me for routine examination has increased.

Such routine clinical examination often reveals unsuspected or neglected disease in the eye, face, or elsewhere. On more than one occasion the fundal picture was the first discovered evidence of latent diabetes and also of grade I, II, or III hypertensive

retinopathy (Keith, Wagener, and Barker, 1939); while rodent ulcer, acne rosacea, and "red eye," which had been receiving treatment as conjunctivitis but was in reality an iritis or uveitis, are not uncommon. Many of these patients had not been to their family doctor for some time. Incidentally, I came across two cases in the series, one a growth on the lip, the other on the tongue, both of which turned out to be secondaries from bronchogenic carcinoma.

Present Investigation

This paper discusses 10,000 consecutive men, women, and children examined by me under the Supplementary Ophthalmic Service of the National Health Service.

The findings are recorded in Table I. Cases which fall under the definition of amblyopia have been selected for analysis.

Incidence of Amblyopia in the Series

The 10,000 patients have been divided into groups of 1,000, and these latter into subgroups of 250. Each group has been analysed according to sex, eye affected, and age. The importance of heredity is referred to below.

The total number of unilateral amblyopias was found to be 527 (5.27%). It is seen (Table II) that in each group of 1,000 individuals there is a heavy crop of unilateral amblyopias. The number varies from 37 among the first thousand to 72 in the eighth thousand. Even in the small blocks of 250 patients at least seven individuals had this disability, while in one block the figure reached as high as 25. Translated into general terms, *out of every* 1,000 *children born* 53 *fail to develop normal binocular vision.*

These are figures for a sample of the population which includes all ages and both sexes. It is interesting to compare them with figures obtained for healthy male adults in the fighting Services. In America, Downing (1945) found that, out of 60,000 airmen selected for service in the U.S. Army, 1,920 had unilateral amblyopia. Theodore, Johnson, Miles, and Bonser (1944) found 4% of 190,012 American soldiers were amblyopic. Irvine (1948) found 4% amblyopes among 5,000 air corps personnel who needed glasses and 1% amblyopes among 10,000 personnel passing out on completion of their service.

Sex Distribution

Tables II and III show that the sexes are fairly equally affected by amblyopia, though there is a slightly higher incidence in the male. This agrees with the findings of Feldman and Taylor (1942).

A study of the sex distribution is important for any understanding of the causation of amblyopia, which is probably related to the hereditary factor. Unfortunately there are scarcely any published data on this point. Even in the case of squint, so much work on which has been published, Waardenburg (1954) lamented the fact that to his knowledge no mass survey of the sex distribution had been recorded.

TABLE II.—*Number of Amblyopias in the Series Divided According to Sex*

Patients Examined Divided into Groups	Amblyopes		
	Male	Female	Total
1– 1,000 (8, 10, 8, 11) ..	22	15	37
1,001– 2,000 (8, 7, 14, 14) ..	20	23	43
2,001– 3,000 (16, 9, 10, 13) ..	20	28	48
3,001– 4,000 (10, 18, 15, 13) ..	21	35	56
4,001– 5,000 (13, 11, 12, 25) ..	27	34	61
5,001– 6,000 (16, 14, 11, 14) ..	23	32	55
6,001– 7,000 (7, 14, 15, 14) ..	19	31	50
7,001– 8,000 (19, 18, 16, 19) ..	30	42	72
8,001– 9,000 (18, 12, 16, 7) ..	24	29	53
9,001–10,000 (10, 15, 16, 11) ..	19	33	52
1–10,000	225	302	527

The figures in parentheses are the number of amblyopes, of both sexes, in each subgroup of 250 in each 1,000.

TABLE III.—*True Sex Distribution of Amblyopia in Series of* 10,000 *Patients*

	Male	Female	Total
Total amblyopias	225	302	527
Average distribution of sexes per 1,000 patients examined ..	415	585	1,000
True sex incidence of amblyopia	5·42%	5·14%	5·27

Heredity

There is a strong element of heredity in amblyopia, but its exact pattern is not known. Amblyopia is a silent condition, and can be diagnosed only by specific examination. As such it is impossible to find by questioning alone whether the relatives of an amblyopic patient are amblyopic, unless they themselves have had their eyes tested. There is often a strong dominant element, as the following case shows.

A woman aged 66, who was about to join her family in Canada, came for a check-up and glasses. With full correction she had R.V. 6/6 (20/20), L.V. 6/24 (20/80). There was no clinical abnormality in either eye. To my query about her left eye, she replied that it had always been

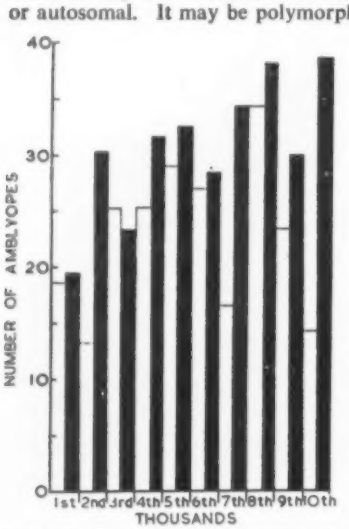
TABLE I.—*Specimen Record of Typical Sight Tests*

Name and Occupation	Sex and Age	Leading Symptom	E.S., H., B.V., E.P.*	C.P.M.F.T.†	1st Glasses?	Retinoscopy	Phoria	Remarks
T. W.; retired ..	M 74	Giddiness on looking quickly to side	Nil	Arteriosclerotic retinopathy, Gr. 1	No	+2·5 + 0·5×90°=6/6 +2·5 + 0·5×90°=6/6 Add + 2·5=J1, J1	Nil	Generalized senile tremor
H. M.; draughtsman	M 31	Shimmering lower field. Hemianopsia. Blurred vision	Headache	Nil	Yes	+0·25×90°=6/5 +0·25×90°=6/5	No convergence deficiency	Migraine ophthalmicus
P. O.; miner ..	M 47	Whirling shadow in front of eyes on reaching open air out of mine	,,	,,	,,	0=6/9 0=6/6	Nil	No nystagmus
Miss M. G.; at school	F 17	Blurred distance vision	Nil	,,	No	Add +1·25=J1, J1 −5·25=6/6 pt; −3·25−2·5×155° =6/6 pt.	,,	Progressive myopia
Miss C. M.; school teacher	F 26	Eyestrain	Headache	,,	Yes	+3·0+1·0×90°=6/18 +0·25+0·5×90°=6/6	,,	R. amblyopia
J. D.; retired ..	M 77	Rainbow round lights	Cataract L. eye	No evidence of glaucoma	No	+1·0=6/6 pt. +1·0=6/60 Add +3·0=J1 (R)		Referred hospital eye service

* E.S.=Eye strain. H.=Headache. B.V.=Blurred vision. E.P.=Pain in one or both eyes.
† C.=Conjunctiva and cornea. P.=Pupil. M.=Media. F.=Fundi. T.=Tension. Phoria=Muscle imbalance and strain.

"lazy" and that both her son, aged 45, and his daughter, aged 7, had "lazy" left eyes. None of the three had ever had strabismus.

On the other hand, such dominance may be irregular and may miss a generation or two. The heredity element may be recessive, X-chromosomal, sex-linked, or autosomal. It may be polymorphous or polygenetic, as in the case with strabismus (Duke-Elder, 1949). It is of the utmost importance that the incidence and pattern of heredity in amblyopia should be studied. Whether or not it is a complication or a predisposing cause of strabismus is immaterial, though it gives added point to the inquiry. It is surprising that amblyopia has not received from the geneticists the attention which has been devoted to such other eye conditions as myopia, retinitis pigmentosa, night-, day-, and colour-blindness, presenile cataract, and acute glaucoma.



Incidence of amblyopia among groups of 1,000 patients. White columns = Right eye. Black columns = Left eye.

Amblyopia More Often Left-sided

Among the 527 amblyopias, 224 (42.5%) involved the right eye, and 303 (57.5%) the left (see Chart). Feldman (1941) found 71% of his series of amblyopias were on the left. In the present series, among the groups of 1,000 patients, in only one (the third) is there a slight preponderance of right-sided amblyopia, while among the subgroups of 250 patients, only 10 times out of 40 do we find amblyopia occurring more often on the right side.

This predilection for the left side probably has a bearing on the nature and causation of amblyopia. It would seem to support Burri's (1942) view that the development of normal simultaneous binocular vision takes place by a process of learning, the progress curve of which is similar to those for learning to walk and talk. The processes leading up to the development of binocular vision are governed by proprioceptive impulses between sight and touch, especially those from the hands.

Age Distribution

When the patients are analysed according to age groups (Table IV) it is seen that in every group there is a significant number of amblyopes. No age, no group, is exempt. The youngest amblyopic patient discovered was 4 years old, the oldest 85. A comparison of these figures with the age distribution of the entire series of patients examined (Table V) also confirms that each age group has a significant quota of amblyopes. Furthermore, both the number of patients examined and the numbers which are found to be amblyopic steadily increase with each decade up to the fifth, after which they diminish steadily. For comparison the figures of the first 7,000 patients are added. It was at this point (7,000 patients examined) that the problem of amblyopia was first reviewed and a communication privately published among interested colleagues.

TABLE IV.—*Number of Actual Amblyopias Discovered, Arranged in Age Groups*

Group of 1,000	Age in Years								Total
	0–10	11–20	21–30	31–40	41–50	51–60	61–70	70+	
1st ..	0	4	6	6	10	7	3	1	37
2nd ..	0	5	7	8	9	6	5	3	43
3rd ..	0	4	7	7	11	7	10	2	48
4th ..	2	6	10	6	9	11	8	4	56
5th ..	1	7	10	17	13	6	5	2	61
6th ..	5	2	8	10	13	10	5	2	55
7th ..	3	4	6	9	12	7	5	4	50
8th ..	8	10	5	13	13	13	4	6	72
9th ..	3	3	6	9	16	8	4	4	53
10th ..	2	7	4	7	9	4	13	6	52
Total	24	52	69	92	115	79	62	34	527

TABLE V.—*Comparative Incidence of Amblyopia per Age Group*

	Age in Years								Total
	0–10	11–20	21–30	31–40	41–50	51–60	61–70	70+	
Total number of amblyopes	24	52	69	92	115	79	62	34	527
Mean number examined per group of 1,000	31	104	129	129	217	214	108	68	1,000
Incidence in entire series ..	7·7%	5·0%	5·4%	7·1%	5·3%	3·7%	5·7%	5·0%	
Incidence in first 7,000	5·0%	4·5%	6·0%	7·0%	5·0%	3·5%	5·0%	4·0%	

A comparison of the age incidence curves of the first 7,000 patients with those for the whole series shows an increase of 50% in the proportion of children under 10 found to be amblyopic. The ratios are 5.0% and 7.7% respectively. During this intervening period more young children were recommended for examination as the implications of amblyopia became more widely known. The figures themselves emphasize the heavy incidence of the condition in childhood.

Diagnosis in Very Young Children

Clearly amblyopia can be tackled only in childhood. Fortunately, although the usual tests for visual acuity are not applicable to children under 5 years, it is possible to diagnose amblyopia even in the youngest baby. A child of 3 or 4 years cannot distinguish fine objects at 6 metres. A baby is "wall-eyed"; and it is only as it grows that the eyes become able to distinguish finer objects, and also ordinary objects at further distances. In seeking out amblyopia in such young children, therefore, it is important to realize that our aim is really to compare the function of the two eyes. If one eye appears to see normally for its age, while at the same time the other eye sees much less, then we suspect that the latter is amblyopic.

I was examining a girl of just under 4 years, with correcting glasses, using a well-known Snellen-type picture chart, the first object on which is a horse representing 6/60, the next line a dog and a cat representing 6/36. In the room near the girl sat her mother with her baby sister, aged 1 year 9 months, on her lap. The girl herself read three rows (6/24) with the left eye. But with the right eye she could barely recognize the horse and could not at all distinguish the dog. I was just about to point to the next object, the cat, when the baby shouted out "dog-gie." This unexpected intervention proved beyond doubt that the

girl should have been able to recognize the dog, and I was able confidently to diagnose her as amblyopic, and to institute treatment immediately.

The acuity of a child's eyes improves with its growth. At any particular time one or other eye will be more efficient than its companion. But in general they should function and develop as a team. Amblyopia is suspected when there is a marked difference between the acuity of the two eyes, and it should be diagnosed when there is as much as two Snellen chart lines between them.

The *family history* is important. Often one parent, especially the mother, and/or one child in the family, is amblyopic in one eye, or has a high degree of hypermetropia in both eyes, or a squint in one eye.

A boy of 2½ was the only member of his family who had not previously been examined. All the others wore glasses, the father for left amblyopia and hypermetropia, the mother for left amblyopia and myopia, and the sister, aged 5, for bilateral hypermetropia with astigmatism. In view of the family history I applied trial occlusion to his left eye for a week and he was perfectly unconcerned; but on covering the right eye, thus forcing him to rely on the left eye, he became immediately uncomfortable and quarrelsome, and stumbled against objects for some days, showing that he was amblyopic in the left eye.

A history of *strabismus fugax*, or *fleeting squint*, is very important. This is the type of squint which appears at certain odd times in the day, usually when the child is tired or towards evening. It often lasts for only a few days at a time, then disappears only to recur on some future occasion. This type of squint may become permanent, may disappear completely, or may continue to be occasional and lurking, until when the child is examined at the age of 6 or 7 he is found to be amblyopic in that eye. Worth (1903, 1921) stressed that no squint, however fleeting, should be regarded as of no significance, but rather was a reason for thorough examination of the eyes.

It is true that many squints if left alone tend to clear up. But they leave behind a trail of permanent amblyopia. Many of these squints are the only evidence that a child's eyes are encountering difficulty in developing binocularly.

After the history the next step is *refraction*. It is better, where possible, to conduct this test without the use of a cycloplegic, as this upsets the balance of the internal muscles of the eye. As Donders (1864) pointed out, refraction is a twofold process involving an examination of (*a*) the structure of the eye in static relation to entrant light rays, and (*b*) the reaction of the eye (accommodative power) to such rays. In my view amblyopia is a disability of function, and structural deviations are incidental to the problem. Discussion of this point, however, is beyond the scope of this paper.

The special *subjective tests* involve an application of the Snellen chart, either in its standard form of individual selected letters or in the various modifications used for illiterate patients and young children. The letter "E" or Landolt's rings are suitable for children of 5 and 4. But for the younger child of 2 or 3 and even 4, nursery Snellen-chart pictures form a more suitable modification of the tests.

Below 3 years, however, such tests become increasingly difficult, and some modification of Worth's marble balls can be used. These are balls of diminishing sizes from 2½ to ½ in. (6.3 to 1.3 cm.) which are flicked on to the floor in such a way that the child cannot tell from the movement of the hands where the ball has gone. The child is then asked to recover the balls, and the number and sizes of these which he is able to recover give a rough indication of his visual acuity. This test can be modified in a number of ways, using such objects as sweets, to mention one medium.

For still younger children diagnostic occlusion is used. When one eye is covered in this way, a child is not unduly bothered if he can see with the other eye. But if the exposed eye is amblyopic, he becomes uncomfortable and tugs at the occlusive dressing, cries, and stumbles against objects. With experience it is possible to detect amblyopic eyes in such very young children.

Where the National Health Service Fails

Although the National Health Service offers free and comprehensive medical care of the entire population, at least 5 out of every 100 children born, and possibly more, still continue to develop one useless eye, with all the hazards and inconvenience this entails. This unexpected gap in the medical eye service is due to the fact that the first compulsory or general examination of children's eyes takes place after they have started school. But unilateral amblyopia is already well established long before this; often before the age of 3, and in the worst cases by the end of the first year. Early ophthalmic examination is indicated if this disability is to be attacked. But as unilateral amblyopia is developmental, and has no presenting symptom, the only way to success is by examining *all* children early and regularly. This is an administrative problem of some magnitude. But the following experience is worth recording.

Not long ago I did a pilot test of some 100 children in order to find out what could be learned from the routine examination of pre-school children, as advocated by many authorities. The patients were unselected. I simply asked as many mothers as were willing, and whose family doctors were agreeable, to bring all their children of school and pre-school ages for ophthalmic examination, including refraction. At the time I could not do more than record the refraction in each case and ask each mother to watch for any untoward development.

The interesting thing is that within a few months three mothers rang up, each to say that her child had been showing signs of strabismus in one eye, chiefly towards the evening or when the child was tired. I examined these children and found that in one, aged 4½ years, there was now a difference of two Snellen chart lines between the eyes. The other two, who were about 3 years old, appeared normal, and I kept them under observation. Later, diagnostic occlusion revealed the presence of early amblyopia in the left eye of one of them. The other remained normal.

The last thing one wishes to do is to encourage undue anxiety or fussiness in parents about their children's eyes. At the same time, once it is generally known that, without developing obvious squint, a child can lose the sight of one eye partially or even totally, the first step will have been taken towards mass attack on the preventable disability of amblyopia.

Summary

Routine examination of a consecutive series of 10,000 patients under the National Health Service disclosed

that no fewer than 527 (5.27%) have one practically useless eye. This condition is colloquially known as "lazy eye." In 1% of all the patients examined one eye was registrably blind, in another 2% the eye had such poor vision as to be quite useless. In the remaining 2% of amblyopic patients the vision was so poor that binocular vision was absent. If this finding were extended to the population at large, it is apparent that, out of every 100 children born, between 5 and 6 are destined to lose the use of one eye.

This condition of unilateral amblyopia is well known throughout the civilized world as a source of wastage of man-power in times of national emergency. Its economic and social disadvantages are equally serious, especially should anything happen to the good eye.

An amblyopic patient is usually ignorant of his disability, relying unconsciously on his good eye. Unfortunately the condition develops in infancy and early childhood, and by the time the child starts school it too often has become permanently established.

In a country with the most comprehensive medical service in the world, it is paradoxical that its young children should be allowed to run the risk of suffering from this grave disability through neglect.

I thank Mr. N. P. R. Galloway and Mr. G. Gordon Napier for their kindness and encouragement, and numerous family doctor colleagues who kindly referred their patients to me, and who otherwise made this investigation possible. My thanks are due also to the editor of the *Journal of the American Medical Association* for special information on visual standards and problems in the U.S.A.

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The *Handbook of Treatment of Acute Poisoning*, by E. H. Bensley and G. E. Joron, of the Montreal General Hospital (2nd ed., pp. 212; E. and S. Livingstone, Ltd., 15s.), is intended primarily for the physician with no special experience of toxicology who is called upon suddenly to treat cases of poisoning. It may also be used as a basis for lectures to students. Although it deals mainly with acute forms of poisoning, with the emphasis on emergency measures, some reference is made to chronic poisoning and the late effects of acute intoxications. A number of industrial poisons are included.

A REVIEW OF 300 PATIENTS WITH HAEMATEMESIS OR MELAENA

BY

J. E. CATES, M.D., F.R.C.P.
Department of Medicine, University of Bristol

During the four years 1953 to 1956 inclusive, 300 patients with haematemesis or melaena were admitted to the Bristol Royal Infirmary: 14 were readmitted on one or more occasions, making a total of 321 admissions. Of these, 308 were emergency admissions, and the other 13 developed the haematemesis or melaena as in-patients. During the four-year period there were 9,355 medical admissions (both emergencies and from the waiting-list), so that haematemesis and melaena accounted for 1 in 30 of these.

Of the 321 admissions (Table I) the bleeding was attributed to a proved or presumed ulcer in 259 (81%). Treatment was medical in 224 cases (with 10 deaths) and was surgical in 35 (with 4 deaths); in most fatal cases, however, death was not from haemorrhage. A cause other than ulcer was diagnosed in the remaining 62 admissions: this group (in which there were 7 deaths) is discussed below.

TABLE I.—*Diagnosis in 300 Patients with Haematemesis or Melaena*

	Ulcer Group							
	Gastric	Duodenal	"Peptic"	Anastomotic or Stomal	Acute Ulcer or Erosion	Total	Other Causes	Total
No. of patients	63	96	38	6	40	243	57	300
,, ,, admissions	66	106	39	6	42	259	62	321
Emergency surgery	10	18	—	1	6	35	6	41
Surgical deaths	1	2	—	1	—	4	—	4
Total deaths	3	10	—	1	—	14	7	21

Before these results can be appraised it is necessary to consider various factors which may influence prognosis.

Age and Sex Incidence

Haematemesis or melaena becomes more common with advancing age (Fig. 1). The frequency increases steadily to the seventh decade; in the eighth and ninth decades the numbers are smaller; out of the whole series of 300, 134 (33%) were 60 years or over. (This increased frequency in the elderly applies both to the ulcer cases and to the others.)

Of the patients with ulcer there were 158 men and 85 women (Fig. 2). Below the age of 70 there were more than twice as many men as women (144 to

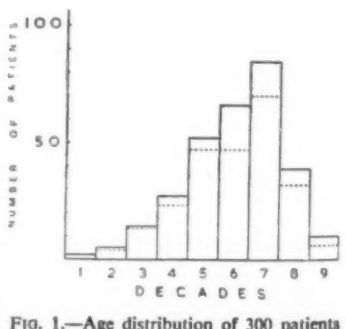

FIG. 1.—Age distribution of 300 patients with haematemesis or melaena from all causes. Those in whom the diagnosis was of some form of ulcer are shown below the interrupted lines.

61), but over that age women outnumbered men (24 to 14). This high incidence among men is found particularly in the group with duodenal ulcer (72 men and 24 women), to a less extent among those with gastric ulcer, and not at all amongst " peptic " ulcers and those with acute ulcer or erosions (Fig. 3). In particular it is in the group with bleeding from duodenal ulceration that men exceed women ; this is so throughout the whole age range, with the difference increasing up to the seventh decade (Fig. 4).

Degree of Severity of Haemorrhage

In assessing how serious was a patient's haemorrhage, whether or not he survived is of little use. This is because with adequate treatment by blood transfusion and emergency operation death from haemorrhage is now quite rare, and death when it does occur is usually due to some associated disease or to advanced age (as is shown below). Probably the best indices of a severe haemorrhage are whether transfusion is needed and whether emergency surgery is needed. Those with coexisting perforation naturally form a more serious group.

It is often held that haemorrhage is more serious in the older male patients and in those who have previously had a haematemesis or melaena. In this series there were 166 admissions of men with bleeding from ulcer: in 114 this bleeding was the first attack, while in 52 there had been a previous episode of bleeding. The severity of the bleeding in these two groups is given separately in Tables II and III.

TABLE II.—*Admissions of Males with First Bleeds from Ulcer*

	Age Group			Total
	-39	40-59	60+	
Total	19	54	41	114
Transfused	10	34	28	72
Emergency surgery	2	12	7	21
Perforation also	—	3	1*	4

* Not operated on.

TABLE III.—*Admissions of Males with Previous Bleeds from Ulcer*

	Age Group			Total
	-39	40-59	60+	
Total	12	15	25	52
Transfused	5	8	16	29
Emergency surgery	—	4	1	5
Perforation also	—	2	—	2

In Table II the details are given of coexisting perforation, of emergency surgery, and of blood transfusion among those 114 admissions of men with no previous haematemesis or melaena: those who underwent emergency surgery numbered 2 of the 19 cases (5%) below the age of 40, while in the fifth and sixth decades there were 12 out of 54 (22%), and over 60 years of age 7 out of 41 cases (17%). (Blood transfusion was also more common in older age groups, but the increase is less marked and is not significant.)

In Table III the same details are given of those 52 admissions of men in whom there had been a previous episode of bleeding. As with those with no previous haemorrhage, the proportion undergoing emergency surgery is higher over the age of 40. In the two groups together (those with bleeding for the first time and those with previous bleeding), emergency surgery was undertaken in 2 of 31 (6%) below 40 years, in 16 of 69 (23%) between 40 and 59, and in 8 of 66 (12%) of 60 and over. On the other hand, these figures do not suggest that, in this series, previous bleeding was associated with any increased severity in this subsequent haemorrhage for which they were then in hospital, for the proportion receiving blood transfusion and undergoing surgery was no higher than in those with no previous history of haemorrhage (Table II).

TABLE IV.—*Admissions of Females, All Bleeds from Ulcer*

	Age Group			Total
	-39	40-59	60+	
Total	18	27	48	93
Transfused	11	19	26	56
Emergency surgery	1	1	7	9
Perforated also	—	—	2*	2

* Neither operated on.

All told, there were 93 admissions of women with bleeding from ulcers (Table IV); 48 of these were 60 years of age and over and 7 had emergency surgery. (There were also 2 of 48 patients in this age group who had also a perforation ; but neither was operated on.) Compared with men in this series it seems that, below the age of 60 at any rate, haematemesis and melaena in women was less often severe.

Nature of Emergency Operation and Findings

Of the patients eventually diagnosed as having haemorrhage from an ulcer, 35 underwent emergency surgery. In five there was an associated perforation ; in four of these bleeding preceded the perforation, and partial gastrectomy was performed in three and local

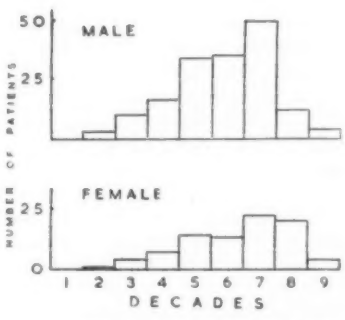

FIG. 2.—Different age distribution in men and women with haematemesis or melaena in whom some form of ulcer was diagnosed.

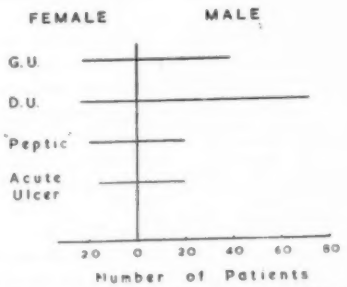

FIG. 3.—Haemorrhage in men from duodenal ulcer was much commoner than in women. Those in whom the site of the ulcer was not determined (" peptic ulcer ") and those with bleeding from acute ulcer were as common in women as in men.

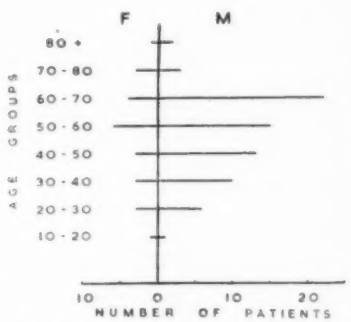

FIG. 4.—Bleeding from duodenal ulcer becomes increasingly common in men until the seventh decade.

suture in the fourth; while in the fifth case perforation was treated by local suture and the haemorrhage followed three days later. There was no perforation in any of the remaining 30, and all had partial gastrectomy to control continuous bleeding.

Of the perforated ulcers, four were duodenal and one was gastric. In the 30 without perforation 7 had a gastric and 14 a duodenal ulcer, while 2 others had both; 6 had subacute ulcers or acute erosions; in the remaining case haemorrhage was from an anastomotic ulcer at the site of an old gastro-enterostomy.

Amongst the whole series of 321 admissions, there were six patients who were submitted to emergency operation and who were diagnosed as not having an ulcer. No cause was found in three of these; the gastric arteries were tied in one, and the abdomen was closed without any further intervention in the other two; and all three recovered.

Six other patients with ulcer underwent surgery (four having a partial gastrectomy) within one to four weeks of admission. As the bleeding had by then ceased and operation was performed for other reasons—for example, to exclude malignancy—these cases are all included among those treated "medically."

Results of Treatment in Ulcer Group

Table V shows the results of treatment in the various age groups of men and women. There were 145 admissions of patients below 60 years of age: 125 were treated medically and 2 died, 20 were treated surgically and 3 died. There were 114 admissions of patients of 60 years or older: 99 were treated medically and 8 died, 15 were treated surgically and 1 died. Among the 166 admissions of men there were 11 deaths, compared with 3 deaths in 93 admissions of women.

TABLE V.—*Results of Treatment in Bleeding Ulcers*

Age Group	Admissions of Men					Admissions of Women				
	Total	Medical		Surgical		Total	Medical		Surgical	
		No.	Deaths	No.	Deaths		No.	Deaths	No.	Deaths
-39	31	29	—	2	—	18	17	1	1	—
40–59	69	53	1	16	3	27	26	—	1	—
60+	66	58	6	8	1	48	41	2	7	—
Totals	166	140	7	26	4	93	84	3	9	—

TABLE VI.—*Deaths in Patients Whose Haemorrhage was from Ulcer*

Sex	Age	Comment
		Medically Treated Cases
F	31	Previously five admissions for bleeds, and a partial gastrectomy. Massive *haemorrhage*
M	58	Died from chest infection
M	62	Pulmonary embolism
M	66	Second *haemorrhage*. Duodenal ulcer and gastric erosions
M	68	In heart failure after coronary. Bled first while in-patient
F	72	Coexisting perforation. Diagnosed, but unfit for surgery
M	77	Perforated after admission. Diagnosed, but unfit for surgery
F	77	" " " Not diagnosed
M	78	Hypertension, coronary ischaemia. Heart failure
M	79	Also carcinoma of colon. Not transfused
		Surgically Treated Cases
M	54	Haematemesis after admission for hypertension. Successful partial gastrectomy. Stroke four weeks later
M	56	Peritonitis after partial gastrectomy for bleeding anastomotic ulcer
M	59	Bled 4 days after closure of perforation. Subphrenic abscess. Massive *haemorrhage* from gastric erosion
M	61	Bled from peptic ulcer after recent abdominal perineal resection for carcinoma; gastrectomy, further *haemorrhage*

Causes of Death

The causes of death in patients with ulcer are given in Table VI. In two cases treated medically and in two other cases in surgical hands the principal or only cause was haemorrhage itself. An associated illness or cardiovascular accident accounted for four others of those medically treated; but the haemorrhage may have predisposed or contributed to death in these cases. In three other medical cases, all over 70 years of age, there was an associated perforation, and in two of these who were judged to be unfit for surgery it is reasonable to attribute to the blood loss part of the shock which rendered these patients unfit for surgery. Of the four deaths among the patients treated surgically, further haemorrhage was the cause in two: in one of these cases, however, the surgery was suturing of a perforated ulcer, and the subsequent bleeding was from fresh acute erosions.

Causes of Haemorrhage or Melaena other than Ulcer

In about one-fifth of the patients in this series the haematemesis or melaena was attributed to some cause other than ulcer: out of the total of 300, there were 57 such patients (Table I and Fig. 5) and they accounted for 62 admissions.

Portal hypertension (10 cases) caused bleeding in all age groups, while bleeding from hiatus hernia (13 cases) occurred only in the middle-aged and elderly.

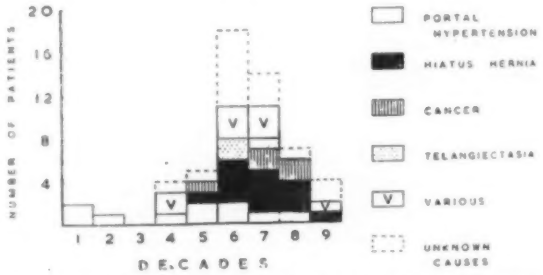

FIG. 5.—The diagnoses made in 57 patients who bled from causes other than ulcer.

Although cancer of the stomach is common it was a rare cause of haematemesis or melaena in this series, there being only five cases. Amongst the group of nine patients shown as "various" are included haemophilia, Schönlein's purpura, uraemia (3 cases), volvulus of the stomach, and an intestinal neuroma. No diagnosis was made in 17 patients. As already mentioned, even at emergency operation no cause was discovered in three; in a fourth no lesion was seen at gastroscopy, and in a fifth who died from a stroke 10 days after admission no intestinal lesion was found at necropsy.

Emergency operations were performed in 4 of the 10 patients with portal hypertension; this was oesophageal transection and ligation in two, portacaval anastomosis in one, and splenectomy with partial gastrectomy in the fourth. All recovered, though one patient died (from haemorrhage) on a later admission. This was the only death from bleeding; of the six other patients who died, four had cancer, one was in uraemia, and one had a stroke.

Seasonal Incidence

Over the four years there were more admissions during the winter: 44 in December, 41 in January, and

30 in February. There were least in the summer: 21 in June and 15 in July. Fig. 6 shows this rhythm; each column represents the total admissions for the month: above the break is the number in the ulcer group, below the break is the number in which bleeding was due to some other disease. (Our hospital records are indexed by the date of discharge or death and not by the date of admission, so that, in fact, the present series consists of patients discharged or dying between January 1, 1953, and December 31, 1956. Therefore, all patients admitted in, say, December, 1952, and who remained in hospital until 1953, are included in this series, whereas those who were admitted in, say, December, 1956, and who were still in-patients on January 1, 1957, have not been included.)

Discussion

Two great advances in medical treatment of haematemesis have been, first, that of adequate fluids by mouth championed by Meulengracht (1935), and, secondly, the use of slow drip blood transfusion introduced by Marriott and Kekwick (1935); the value of these two principles of treatment was clearly proclaimed by Avery Jones (1947). Less surely established is the role of emergency surgery, and the purpose of this present review was partly to collect evidence about this.

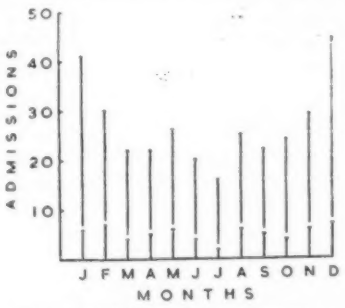

FIG. 6.—Admissions for haematemesis or melaena were more common in the winter months of December, January, and February, and least common in the summer.

It is widely recognized that, whatever the treatment, the results in haematemesis are profoundly affected by age, and to a less extent by sex and the nature of the underlying lesion. Moreover, the endemiology of ulcer varies in different parts of the country, and changes as time goes by. So to enable our results to be compared with those of others, both published and in future, this information about our patients has been included in this report.

Effects of Age

The incidence of peptic ulcer increases with age until about 55 (Doll, Jones, and Buckatzsch, 1951), and the steady rise in haematemesis is in keeping with this. After that age the incidence of ulcer decreases (Doll *et al.*, 1951), though haematemesis, at least in this series, becomes more common. In Fig. 1 the numbers in the eighth and ninth decades are fewer, but, of course, the number is also lower in the general population, and if allowance is made for this the incidence in all the groups over 60 is constant.

In the 1951 census 16% of the population were 60 years old or more, so the proportion of 33% of that age group in our series reflects an actual prevalence of bleeding in the elderly. There is also a steady increase in the elderly in the general population. The effect of these two factors may be seen in the observation of Avery Jones (1957) that the numbers of those over 60 years in his very large series have been increasing in recent years: thus there were 33% between 1941 and 1946, 38% between 1947 and 1951, and 40% in 1952 to 1954.

Amongst the elderly haematemesis and melaena prove to be much more dangerous than in those who are younger. In the experience of Lewin and Truelove (1949) the death rate in those without previous haematemesis was only 5.1% for those under 50, compared with 29% for those above that age. Avery Jones (1957) in his larger series showed a sharp increase in mortality at 60: in the period 1951 to 1954 this mortality for all ulcer cases under 60 years was only 2%, compared with 16.5% for those over that age. In our series the results in the corresponding age groups are 3.4% and 9%.

It is acknowledged that the reason for the increased mortality in the older age groups is not that the bleeding is more severe, for death from haemorrhage is most unusual, but rather that it is largely due to associated diseases, particularly chronic chest diseases, and the high incidence of complications after admission such as pulmonary embolism and urinary or other infections (Avery Jones, 1956). The facts in Table VI provide ample support for this generalization. All the same, a haemorrhage in an elderly patient must contribute to the death in many of these cases; the accompanying fall in blood pressure must be more serious when there is coronary or cerebral atheroma; and, as Gunz, Gebbie, and Dick (1954) have shown, timely transfusion is often of benefit in these patients when they develop symptoms of insufficient coronary blood supply.

Sex

The different incidence of bleeding from ulcer in men and in women conforms with the different prevalence of the ulcers. Thus the relative immunity of women to ulcer until the menopause (Doll *et al.*, 1951) is reflected in the corresponding lower incidence of haematemesis over the same span (Fig. 2). There is a higher incidence of chronic ulcers in men, but the incidence of acute erosions in the two sexes is equal (Avery Jones and Pollack, 1945); likewise in the present series, bleeding from the various lesions seems to be distributed amongst the sexes according to the same pattern (Fig. 3).

Our results in women were better than in men (3 deaths out of 93, compared with 11 out of 166); that this was not entirely due to chance is suggested by the results of Avery Jones (1956), who also found them to be better in women. Why this should be is not certain, but in our series less use was made of blood transfusion and of emergency surgery in women, so the haemorrhage itself seems less often to have been severe.

Previous Bleeding

It used to be believed that a previous episode of bleeding indicated that the patient's ulcer was likely to be deep and scarred and haemorrhage might more readily persist. More recently Lewin and Truelove (1949) found that a history of previous haemorrhage had no bearing on the immediate outcome. As stated above, it seems that the outcome is of little value in assessing the severity of a patient's haemorrhage, because very few of our patients died from haemorrhage. Those with severe haemorrhage now have transfusions

and, if need be, undergo surgery. If these procedures are good evidence of severity there is no indication (Tables II and III) that a history of previous haemorrhage made matters any more serious. As a corollary these same criteria support the conclusion of Lewin and Truelove (1949) that the worse results in the older age groups are not related to a higher frequency of previous haemorrhage.

Emergency Surgery

Among the 259 admissions for bleeding from ulcers there were 14 deaths (5.4%). This figure is as low as has been achieved elsewhere. The results do not seem to be due to a favourable selection of patients, for the composition of the series is materially much the same as that of Avery Jones (1957) except that we had slightly fewer old patients. In 35 of the 259 admissions (13.5%) an emergency operation was done, and in 33 of these the procedure was partial gastrectomy. In men between 40 and 59 years old the proportion undergoing operation was 23%. Fraenkel and Truelove (1955) reported that the death rate in their series has fallen from 18.8% to 5.6%, and attribute this to their increased use of emergency surgery; they now treat as many as one in six patients by emergency operation. Ogilvie, Cardoe, and Bentley (1952) reported that in their cases, where the proportion treated surgically has been 10%, the mortality was 5%. Avery Jones (1957), however, has found no fall in the overall mortality since emergency partial gastrectomy was introduced as a policy, though he is convinced that there is good reason for this operation in selected cases.

From the causes of death (Table VI) it is apparent that in our series more frequent surgery could not be expected to reduce the mortality much further.

As emergency partial gastrectomy carries its own risk, it is self-evident that the best results can be achieved only when patients selected for surgery are all those who would have a worse prognosis if they were treated medically. The criteria that have been laid down to guide others when to operate vary a little in detail, but the principles are the same. Thus, continued bleeding after 24 hours in hospital is used as a criterion by Ogilvie *et al.* (1952) (though some might feel this rather rigid); Avery Jones (1957), from his own experience and that of others, adopted a policy whereby operation was performed "especially on patients with known chronic ulcer whose age was over 40 and who had a brisk recurrent bleeding after admission."

In this series there has been no question of a uniform policy adopted alike by all physicians or surgeons; but it is a principle to seek surgical opinion early in any severe haematemesis, and for both the medical and the surgical attendant to review the need for surgery if bleeding continues or recurs. An essential part of this treatment has proved to be the routine use of the 15-minute pulse chart and the careful instruction of the nursing staff to report promptly any material increase in pulse rate. In this way patients needing surgery can be detected and so operated on at any hour of the day or night.

When both perforation and haematemesis are present, surgical treatment is desirable if the patient can be made fit enough. But, as others have shown (Slater, 1951), the double diagnosis is hard to make when shock from haemorrhage is severe.

Causes Other than Ulcer

In our series the proportion due to causes other than ulcer (57 of 300 cases) is a little higher than in the large series of Avery Jones (1957). This is partly due to the interest of the professorial surgical unit in portal hypertension, for a few of these cases are admitted as emergencies with haematemesis. Our figures are otherwise too small and the cases too varied to justify further comment.

Seasonal Variations in Hospital Admissions for Haematemesis and Melaena

The first report that peptic ulcers are more likely to perforate in the winter is attributed to Brunner (1903), and this has been amply confirmed by Illingworth, Scott, and Jamieson (1944). The results in our series show that the same rhythm is now clear in the incidence of bleeding from ulcers. This finding is likely to be influenced somewhat by unknown factors, such as a possible increase of old people in Bristol in the winter and their departure during the summer holiday season, but the large variations in numbers in Fig. 6 are unlikely to be due to such factors and probably reflect the aggravation of ulcers in the winter, the causes of which as yet have been only surmised (Illingworth, 1952).

Summary

A total of 300 patients with haematemesis or melaena have been reviewed.

The incidence rose in the older age groups; 33% of the series were 60 years of age or older.

Peptic ulcer or erosion was diagnosed in 81%.

Bleeding did not seem to be more serious in patients who had bled in the past.

The proportion of ulcer patients who had a partial gastrectomy as an emergency for continued bleeding was greater in those over 40 years of age: in men between 40 and 59 the rate of this emergency operation was 23%.

Among the 259 admissions for bleeding ulcer there were 14 deaths (5.4%).

Four patients with ulcer died from continued haemorrhage, two had been treated medically and two surgically.

Over the age of 60 the major hazard in patients with bleeding ulcers was from their associated diseases.

In this series there were about twice as many admissions in the winter as in the summer.

All members of the consulting staff of the Bristol Royal Infirmary allowed me to report their cases. Mr. A. E. J. Turner, records officer, and his staff in the United Bristol Hospitals, undertook the heavy task of collecting together the records with the aid of the diagnostic index. Dr. P. C. Farrant, Dr. K. R. Gough, and Dr. H. de V. Heese collaborated in preparing punch-cards; I owe them my grateful thanks. I also thank Professor C. Bruce Perry for his encouragement and advice.

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RELIEF OF POST-OPERATIVE PAIN

BY

E. COPE, M.D., M.R.C.O.G.
Consultant Obstetrician and Gynaecologist, Dudley Road Hospital, Birmingham

AND

P. O. JONES, M.A., M.B., M.Sc., A.R.I.C.
Medical Research Department, The Wellcome Foundation

Relief of pain following major surgery is necessary for two main reasons: (1) the patient's general comfort; and (2) to enable limb, trunk, and breathing exercises designed to prevent post-operative complications, particularly thrombosis and embolism, to be carried out satisfactorily. In an endeavour to find the best available means of relieving post-operative pain a study was made of three recently introduced analgesics—dihydrocodeine, dipipanone, and dextromoramide (R 875)—to determine if these offered any advantage over conventional analgesics, such as morphine.

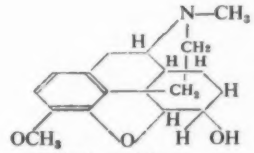
Chemistry and Pharmacology

Dihydrocodeine, a close chemical analogue of morphine, was first reported to be a potent analgesic in the experimental animal by Eddy and Small (1934). Gravenstein *et al.* (1956) showed that 30 mg. of dihydrocodeine was approximately equianalgesic with 10 mg. of morphine, with a slightly shorter duration of action, but with substantially fewer side-effects. These workers found that increasing the dose from 30 to 45 mg. did not appreciably enhance the analgesic effect.

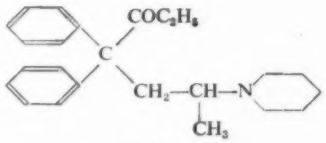
Dipipanone is related chemically to methadone, and its analgesic properties were first described by Ofner *et al.* (1950). Cahal (1957) showed that a dose of 25 mg. raised the pain threshold in man to the same extent as did 10 mg. of morphine. Its use in doses of this order for the relief of pain due to acute and chronic medical conditions and in post-operative pain was reported by Gillhespy *et al.* (1956) and its use as an analgesic in labour by Coleman *et al.* (1957). In these studies adequate relief of pain was obtained in about 95% of cases, with an incidence of side-effects of less than 5%.

Dextromoramide, chemically a new type of analgesic, was synthesized and its analgesic properties first described by Janssen and Jageneau (1957). Although weight for weight twenty times more potent than morphine in the experimental animal, its ability to raise the pain threshold in man was found by Cahal (1958) to be approximately the same. Its use in the treatment of pain in doses up to 10 mg. was reported by Soupault *et al.* (1957) and by David and Deligné (1957).

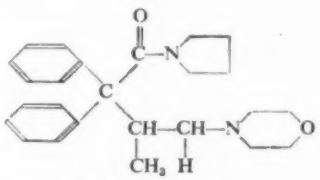
The structural formulae of the three analgesics are as follows:



Dihydrocodeine



Dipipanone



Dextromoramide

Method and Materials

As papaveretum, the post-operative analgesic already in use by us for a number of years, was reliable, and as its analgesic properties could be attributed to its content of morphine, it was used in preference to morphine itself as the standard with which to compare the other drugs. It was thought that the safest form of trial consistent with a fair comparison of these four potentially dangerous drugs was to treat similar series of post-operative patients with each of them in random order. The number of patients treated, the nature of the operations performed, and the order in which the analgesics were given are shown in Table I. The four series of cases treated were similar with respect to the patients' mean age and weight, the type and duration of operation, the surgical techniques used, and pre-operative and post-operative care.

TABLE I.—*Details of Cases Treated*

Order	Analgesic	Major Gynaecological Surgery	Lower Segment Caesarean Section	Total Cases
1	Papaveretum 20 mg. ..	100	25	125
2	Dipipanone 25 mg. ..	100	25	125
3	Dihydrocodeine 50 mg. ..	40	20	60
4	Dextromoramide 10 mg. ..	55	25	80
	Total ..	295	95	390

The dose level chosen for each drug was that which on the basis of the available clinico-pharmacological data would be expected to give a good level of analgesia with minimal side-effects. These were: papaveretum 20 mg., dipipanone 25 mg., dihydrocodeine 50 mg., and dextromoramide 10 mg. These doses were approximately equianalgesic with morphine 10 mg. (1/6 gr.) and the drugs were administered subcutaneously every six hours

for the first 36 hours after operation. Neither the patients receiving the drugs nor the nursing staff assessing pain relief had prior knowledge of the nature of the compounds under investigation.

Objective and subjective assessment of pain relief was made at 15-minute intervals during the first hour after injection and every hour thereafter. Relief of pain was classified broadly as excellent, moderate, slight, or nil. Use of the term "complete relief" (Gillhespy *et al.*, 1956) has now been abandoned by us as inappropriate, for analgesia invariably takes some time to develop and pain gradually reappears after about the fourth or fifth hour.

Results

Pain relief produced by the four drugs under investigation and the incidence of side-effects in relation to the total number of doses given are shown in Tables II and III respectively. No important differences were observed to occur between the series of post-operative gynaecological cases and those which had undergone caesarean section. Therefore the figures for the two types of case have been combined.

TABLE II.—*Relief of Post-operative Pain by Subcutaneous Injection*

Analgesia	Papaveretum 20 mg.	Dipipanone 25 mg.	Dihydrocodeine 30 mg.	Dextromoramide 10 mg.
Excellent ..	115 (92%)	114 (91·2%)	21 (35·0%)	67 (83·8%)
Moderate ..	10 (8%)	10 (8·0%)	34 (56·7%)	11 (13·7%)
Slight ..	0	1 (0·8%)	5 (8·3%)	2 (2·5%)
Nil	0	0	0	0
Total ..	125	125	60	80

TABLE III.—*Side-effects after Subcutaneous Injections*

Side-effects	Papaveretum 20 mg.	Dipipanone 25 mg.	Dihydrocodeine 30 mg.	Dextromoramide 10 mg.
Sweating	22 (3·0%)	28 (3·7%)	10 (2·9%)	37 (8·2%)
Giddiness	14 (1·9%)	13 (1·7%)	5 (1·4%)	201 (44·2%)
Nausea only ..	4 (0·5%)	6 (0·8%)	0	0
Nausea and vomiting	25 (3·4%)	6 (0·8%)	12 (3·5%)	25 (5·5%)
Headache	0	1 (0·1%)	96 (27·6%)	9 (1·9%)
Apnoea with unconsciousness	0	0	0	3 (0·7%)
Total side-effects ..	65 (8·8%)	54 (7·1%)	123 (35·4%)	275 (60·5%)
Total No. of doses ..	732	750	348	455
No. of patients ..	125	125	60	80

When administered subcutaneously there was no significant difference between the analgesics in the time of onset of analgesia or in its duration of action. Slight relief occurred in each instance in 10 minutes and maximum relief in about 20 minutes. After four and a half to five hours pain gradually returned, and increased in intensity until at six hours a further dose of analgesic became necessary. Marked differences existed, however, in the level of analgesia achieved and in the total incidence of undesirable side-effects. The significance of the differences between the various pairs of analgesics is shown in Table IV.

TABLE IV.—*Comparison of Pairs of Analgesics with Respect to Analgesia and Side-effects*

	Best Analgesic Effect	Lowest Incidence of Side-effects
Papaveretum and dihydrocodeine ..	Papaveretum. $P<0.05$	Papaveretum. $P<0.05$
,, dipipanone	No sign. diff.	No sign. diff.
,, dextromoramide ..	,, ,,	Papaveretum. $P<0.05$
Dihydrocodeine and dextromoramide	Dextromoramide. $P<0.05$	No sign. diff.
,, dipipanone ..	Dipipanone. $P<0.05$	Dipipanone. $P<0.05$
Dipipanone and dextromoramide ..	No. sign. diff.	Dipipanone. $P<0.05$

Sedation—sometimes a desirable and sometimes an undesirable property of an analgesic but difficult to distinguish reliably from the effects of pain relief—was judged mainly by the patient's ability to get off to sleep at night without the use of a hypnotic. Dipipanone 25 mg. and dihydrocodeine 50 mg. did not induce sleep, although the latter produced drowsiness in some cases, and had to be supplemented at night with amylobarbitone sodium 3 gr. (0.2 g.). Adequate sleep was induced both with papaveretum 20 mg. and dextromoramide 10 mg., and amylobarbitone sodium was not required.

Severe respiratory depression amounting to apnoea occurred in three cases receiving dextromoramide. After the first of these the dose of this analgesic was reduced from 10 to 7.5 mg., and when two further cases occurred in rapid succession its use as a post-operative analgesic was discontinued. The details of these three cases were:

Case 1.—A woman aged 49 had undergone a total hysterectomy for uterine fibroids and appendicectomy. Before operation her general health had been good and there was no history of allergic disease or drug sensitivity. Post-operatively her condition was satisfactory, and dextromoramide, 10 mg. subcutaneously, was given six-hourly to relieve pain. The analgesia was good and the patient slept for two to two and a half hours following each injection. Twenty minutes after the fifth injection her respiration was seriously depressed and she became apnoeic and unconscious. Her blood pressure was normal (120/80) and her pulse rate 70 and regular. Continuous oxygen was immediately administered and resuscitation measures were instituted. Nalorphine was temporarily withheld, but intravenous nikethamide 1 ml. and aminophylline 500 mg. were given. Within five minutes respiration restarted spontaneously. The patient was fully conscious after 30 minutes and completely recovered in one hour.

Case 2.—A healthy woman of 39 underwent a Manchester type pelvic floor repair operation for prolapse. Five hours after the operation, when she had fully recovered from the anaesthetic and was in good general condition, 7.5 mg. of dextromoramide was given subcutaneously. Ten minutes later there was slight relief of pain and she was awake and well. Twenty minutes after the injection she was unconscious and apnoeic. The pulse was just palpable and the rate 70 and regular. She was pale but not cyanosed; the skin was warm and there was no excessive perspiration. She was lowered from the Fowler position and the foot of the bed was raised. Continuous oxygen was administered and resuscitation carried out. Nalorphine was withheld, but nikethamide 2 ml. was given intravenously and was quickly followed by a spontaneous return of respiration. This was slow at first but adequate after 10 minutes. Full consciousness was regained after 30 minutes, and in 45 minutes she was comfortable and co-operative, but felt drowsy.

Case 3.—A healthy woman aged 70 who had undergone a Manchester type pelvic floor repair operation was given 7.5 mg. of dextromoramide subcutaneously five and a half hours later. She appeared to have recovered completely from the anaesthetic and her general condition was good. Ten minutes after the injection she had slight relief of pain. After 20 minutes there was moderate relief of pain, she was very drowsy, her pulse rate was 80, and there was no undue respiratory depression. Thirty-five minutes after the injection her respiratory rate fell to 6 a minute and she became unconscious. Her pulse rate was 110–120 and blood pressure 180/110. She did not become apnoeic. In a few

minutes her respiratory rate increased and in 10 minutes she recovered consciousness. She remained drowsy for three hours, but was quite co-operative when aroused.

In this series of 390 cases there was only one death which was attributable to post-operative complications.

A coloured woman aged 37 with a bulky fixed retroverted uterus bound down in the pouch of Douglas by numerous adhesions distorting the Fallopian tubes. At operation the adhesions were divided, the tubes were rendered patent, and the uterus was fixed by means of a Gilliam suspension. Post-operatively dihydrocodeine, 50 mg. six-hourly, was given and provided moderate relief of pain. However, she was apprehensive and reluctant to carry out her exercises. Although she had been ambulant from the second post-operative day and had seemed well, she suddenly had a massive pulmonary embolism on the eighth day. There were no warning symptoms or signs, and she died in 20 minutes.

Discussion

Intravascular thrombosis, with the possible sequel of pulmonary embolism, is perhaps the greatest danger to the post-operative patient now that wide and more rational use of blood transfusion and modern developments in chemotherapy have minimized the danger from other complications (Bourne and Williams, 1953). Statistical figures show a great variation, but at present pulmonary embolism accounts for 15% of all post-operative deaths, and probably 0.25% of patients submitted to gynaecological operations die from this cause (Shaw, 1954). Although thrombosis and embolism do not usually manifest themselves until the eighth to the twelfth post-operative day, it is probable that thrombosis starts in the immediate post-operative period, when the circulating thrombokinase is at a maximum and the patient is least mobile.

While opinion on this point is not unanimous it would seem that one of the best safeguards against such a catastrophe is to teach the patient limb, trunk, and breathing exercises prior to operation and to continue these as soon as he is sufficiently recovered from the anaesthetic. Early ambulation is also said to reduce the incidence of post-operative pulmonary embolism (Shaw, 1954). With these methods the number of deaths from post-operative pulmonary embolism has been 1 in the series of 390 cases reported in this paper and 3 in the last 1,700 major gynaecological operations performed by one of us (E. C.), an incidence of less than 0.2%.

To obtain the necessary co-operation from the patient adequate pain relief without drowsiness, respiratory depression, or side-effects such as giddiness, nausea, and vomiting is essential. Persistent vomiting is thought to be particularly undesirable, for this causes dehydration, with increased haemoconcentration and a greater liability to thrombosis.

The order in which the four drugs investigated satisfied the criteria of a good post-operative analgesic were: dipipanone, papaveretum, dextromoramide, dihydrocodeine. Papaveretum and dipipanone both produced excellent relief from pain and a low incidence of side-effects. The former, however, produced sleep in 116 out of 125 patients following the first three doses, and in many cases the patients were too drowsy on the day following operation to co-operate fully in the performance of exercises. Apart from this, vomiting was the only important side-effect of papaveretum, although in only about one-half of the instances reported could this be definitely ascribed to the drug. Giddiness with both papaveretum and dipipanone, when it occurred, did so on the second post-operative day, when the patients tended to be in a more upright position.

Dextromoramide, while affording good analgesia, produced a high incidence of side-effects, in particular giddiness, sweating, and respiratory depression. In the three cases here reported the period elapsing between injection and the onset of respiratory depression excludes the possibility that the drug may accidentally have entered a vein. Although it can readily be fully reversed with nalorphine (Janssen and Jageneau, 1957; A. F. Green, 1958, personal communication) severe respiratory depression amounting to apnoea following the subcutaneous administration of an analgesic must be regarded as a disadvantage.

As a result of previous experience with dihydrocodeine 30 mg., the dose level used in this investigation was raised to 50 mg. Even so, its analgesic effect was significantly less than that of the other drugs. Increasing the dose from 30 to 50 mg. did not appear substantially to enhance the analgesic response, and in this respect our findings agree with those of Gravenstein *et al.* (1956).

It was not possible in this investigation to make a reliable study of side-effects, such as constipation and addiction, which arise during long-term administration and which may be of considerable importance when the drugs are used for the relief of chronic pain.

Summary

In an endeavour to find the best available analgesic for the control of post-operative pain a study was made of three recently introduced analgesics—dipipanone, dihydrocodeine, and dextromoramide—to determine if these offered any advantage over conventional analgesics based on morphine.

The order in which the four drugs investigated satisfied the criteria of a good post-operative analgesic were: dipipanone 25 mg., papaveretum 20 mg., dextromoramide 10 mg., and dihydrocodeine 50 mg. The importance of adequate pain relief in the immediate post-operative period and its possible effect on the incidence of thrombo-embolism are discussed.

We thank Dr. P. A. J. Janssen, of Eupharma, Turnhout, Belgium, for the supplies of dextromoramide (R 875) used in this investigation, and Sisters M. Higgins, J. Wood, and E. Parry, of the Dudley Road Hospital, Birmingham, without whose co-operation this work could not have been carried out.

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ACETAZOLAMIDE THERAPY WITH RENAL COMPLICATIONS

BY

D. WYNNE DAVIES, M.B., M.R.C.P.

Senior Medical Registrar, United Cardiff Hospitals

Acetazolamide ("diamox") is widely used in the treatment of heart failure, epilepsy, and glaucoma. Although this drug is chemically a heterocyclic sulphonamide, there have not been many reports of renal complications following therapy. A number of cases have been recorded with renal colic whilst receiving treatment, but some of these were shown to have renal calculi. Becker and Middleton (1955) reported a case with an exacerbation of renal colic, in a series of 70 cases of glaucoma treated for up to 15 months; and Scheie (1955) described two cases treated for glaucoma which had symptoms of renal calculi, but these might have been present before therapy was instituted. Persky *et al.* (1956) reported the cases of two patients on long-term therapy for glaucoma, who had renal calculi, and that of a third patient, who had renal colic after two weeks of treatment, but a calculus was not demonstrated. They also quoted a personal communication (Leopold) concerning two patients with calculi receiving this drug. Barraquer and Escribano (1957) recorded typical renal colic in 30 patients among 300 treated for glaucoma, and five of these had copious haematuria.

It seems appropriate to record a case in which the repeated administration of acetazolamide was followed by recurrent renal complications.

Case Report

The patient, a professional man aged 28, had been subject to major and minor fits for 12 years, attributable to idiopathic epilepsy, and had regularly taken various anticonvulsant drugs. In addition, acetazolamide, 250 mg. daily, was first prescribed in March, 1957, and the incidence of his fits diminished. Without any previous history of renal disorder, he developed severe colicky pain, radiating from the left loin to the left testis, five weeks after the institution of the new drug. This attack lasted half an hour, and no urinary abnormality was noted.

One week later a similar attack of left renal colic occurred for 12 hours, and this time a small quantity of blood-stained urine was passed. He was well for a further six days and then developed right renal colic, which recurred intermittently until his admission to hospital four days later. Between the spasms he had dysuria and a constant dull ache in the right loin and right testis. The urine was not blood-stained, and, as before, no calculus or gravel was passed.

On admission (May 13) slight tenderness in the right renal angle was the only abnormal physical sign. He was afebrile and the blood pressure was 130/80. A catheter specimen of urine was sterile, free from albumin, and normal on microscopy. An intravenous pyelogram showed that the dye was not concentrated by the right kidney, but the density of the right renal shadow appeared to be slightly increased. The dye was excreted by the left kidney in diminished concentration. Calcified mesenteric glands were noted in the central abdomen, but no calculi were seen.

Retrograde examination of the urinary tract was performed by Mr. D. B. E. Foster on May 14. Cystoscopy revealed a normal bladder. Following right ureteric catheterization and irrigation with normal saline, a coagulum (described as "a sludge") was dislodged, resembling altered blood, which appeared to be obstructing the urinary flow. Similar material was obtained from the left ureter, but less in quantity. Subsequent retrograde pyelography revealed no significant abnormality in either urinary tract, and there was no evidence of renal or ureteric calculi. Sterile specimens of urine were collected from both ureters before and after irrigation. Crystals were not found on microscopy, and the only abnormalities seen were numerous red blood corpuscles and occasional leucocytes. Acetazolamide therapy was discontinued without recurrence of urinary symptoms in hospital. He remained afebrile, and his daily urinary output was normal. An intravenous pyelogram one week later showed normal dye concentration and excretion by the right kidney, whereas concentration by the left kidney was still deficient.

After discharge from hospital on May 28 he returned to his home in another part of the country. Acetazolamide was not used again until the end of July, when he was given 250 mg. daily because of unsatisfactory control of his epilepsy. Six days later he developed an aching testicular pain and the drug was discontinued, with subsequent relief from pain. He was finally given acetazolamide 65 mg. daily in another centre in November, and after 10 days similar aching testicular pain occurred, followed by an attack of left renal colic, which lasted 10 hours. The drug has not been used again, and he has had no further renal colic.

Discussion

The third case of Persky *et al.* (1956) had certain features in common with our patient. They described a woman with glaucoma, aged 63, who was admitted to hospital with left renal colic, two weeks after the beginning of acetazolamide therapy (250 mg. four times daily). She had haematuria and frequency, and was tender in the left flank. The only microscopical abnormality recorded was red blood cells in the urine. Intravenous pyelograms before ureteric catheter drainage showed delayed excretion on the left, but afterwards normal excretion was demonstrated. No calculi were seen, but it was presumed that a small calculus had been passed, as there was haemorrhage and oedema of the left ureteric orifice. A blood clot, however, could have caused ureteric obstruction, as in our patient.

Since our patient also did not have crystalluria, the case described by Glushien and Fisher (1956) is particularly significant. A course of acetazolamide (250 mg. thrice daily for four days) had been prescribed for oedema complicating Hodgkin's disease, and at necropsy, 24 days later, renal lesions attributable to the drug were discovered. He had not taken any other form of sulphonamide drug. Microscopy revealed crystals in the renal tubules which resembled crystals that were obtained by the recrystallization of acetazolamide in acid solution. In spite of these and other renal changes, there had been no evidence of significant nitrogen retention or urinary suppression, and urinalysis had been entirely normal.

Bertino *et al.* (1957) found similar crystals in the renal tubules at necropsy in a case of the nephrotic syndrome, in which a total of 3 g. of acetazolamide had been given over nine days, 11 weeks before death.

The alternation between left and right renal colic which occurred in our patient was also noted by Barraquer and Escribano (1957) in one of their 30 cases.

There seems to be no doubt that the administration of acetazolamide to our patient caused his repeated attacks of renal colic. This is strongly suggested by the sequence of events, the absence of symptoms when the drug was withheld, and the negative previous history. There was evidence neither of calculus nor of infection of the urinary tract. The patient was most impressed by the beneficial effect of the addition of acetazolamide

to his anticonvulsive therapy, and he is disappointed that he has been unable to continue to take this drug.

ADDENDUM.—Since this paper was submitted, a man aged 57, with glaucoma, has been admitted to Llandough Hospital with typical right renal colic, which occurred during long-term acetazolamide therapy (250–500 mg. daily for three months). The pain lasted 36 hours and there was no oliguria. The previous history and physical findings were not suggestive of renal disorder. Numerous red blood corpuscles and occasional leucocytes were seen on microscopical examination of the urine, which was sterile, and an intravenous pyelogram was normal. My thanks are due to Mr. D. B. E. Foster for inviting me to see this patient.

Summary

A case of recurrent renal colic attributable to the repeated use of acetazolamide is described. One episode of unilateral suppression of urine was successfully treated by ureteric catheterization. Similar cases in the literature are discussed in brief.

I am indebted to Dr. Byron Evans for his permission to publish this case and for his advice. My thanks are also due to Dr. G. de B. Hinde for his help in the interpretation of the radiographs.

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Medical Memorandum

Acute Dystonic Reaction to Perphenazine

Phenothiazine derivatives of increasing variety are now in use as tranquillizers and anti-emetics and in the treatment of psychiatric disorders. The toxic effects of these drugs may occasionally cause alarm and diagnostic confusion to the uninitiated, and we are prompted to report the following case in which a dramatic picture suggestive of tetanus followed the use of a small dose of perphenazine (" trilafon ").

CASE REPORT

The patient, a girl aged 18, had been treated unsuccessfully with dimenhydrinate for vomiting of pregnancy. At 10 weeks, treatment was begun with perphenazine, 4 mg. twice daily. At 6 a.m. the next day she complained of aching at the root of the jaws and difficulty in opening her mouth, but as the vomiting had been relieved she took a third tablet.

A few hours later she reported in the surgery. Her head was tilted backwards and to one side and her jaw was held open. Her facies was immobile and vacant. Although she could talk, she could not maintain her mouth in the closed position. She said her eyes were trying to roll upwards and she still had aching in the jaws. Her gait was normal and there was no tremor. She had no vertigo or headache and was mentally normal, alert, and acutely embarrassed by her " foolish appearance."

The diagnosis of a drug reaction was made. Pethidine, 50 mg., was given intramuscularly, and after 30 minutes the posture had relaxed and the facies had improved. During the next six hours, however, the symptoms of dystonia returned in spasms of increasing severity alternating with partial relaxation. The features were now clenching of the jaws and head retraction. At 7 p.m. she was found in a position of opisthotonos, with strong spasm of all the spinal muscles. There was severe trismus and risus sardonicus, the eyes were deviated upwards, and the brow was corrugated. She was fully conscious and anxious, and intimated that she had pain in the neck.

Apart from the upward deviation of the eyes, the picture was now typical of tetanus, and there was a recent history of chronic sepsis in the leg. Confidence was shaken in the diagnosis of an iatrogenic disorder, and after another dose of 100 mg. of pethidine she was transferred to hospital.

The pethidine again appeared to induce rapid relaxation. On arrival in hospital an hour later she was drowsy and depressed, but there was no trace of dystonia, and she could touch her toes. Full neurological examination was negative. As her story was reminiscent of an oculogyric crisis, signs of extrapyramidal disorder were particularly sought, but were absent.

Subsequently the use of phenothiazine drugs was avoided and there was no further evidence of any abnormality of physical or mental behaviour.

COMMENT

Perphenazine (" trilafon " ; 1-[3-(2-chloro-10-phenothiazinyl) propyl]-4(2-hydroxyethyl) piperazine) is closely related to prochlorperazine (" stemetil " ; 1-[3 (3-chloro-10-phenothiazinyl) propyl]-4-methyl piperazine). Various bizarre reactions which were thought to be peculiar to stemetil have been reported by the manufacturers. These include lip tremors, athetotic movements, trismus, and torsion of the spine with painful spasms of spinal muscles which may amount to opisthotonos. Hare (1958) has drawn attention to the very rare occurrence of similar symptoms, including head retraction, due to chlorpromazine. In addition mild features of Parkinsonism may occur with all drugs of the phenothiazine group. Although the more dramatic manifestations may be aggravated by stress and partly alleviated by commands, there is no doubt that they represent a true drug reaction and are not hysterical in nature. They appear to be related to high dosage and to be entirely reversible.

Acute dystonia following perphenazine has been noted previously (Shanon *et al.*, 1957). Other reports, however, have stressed its low toxicity in a dose range of 8–16 mg. daily, mild features of Parkinsonism occasionally occurring with daily dosage above 40 mg., while 72 mg. has been given for long periods in psychiatric practice (O'Reilly *et al.*, 1957 ; Schultz and Henderson, 1957). The reaction we have described after a total dose of 12 mg. is therefore remarkable. Although no other features of Parkinsonism were present, it appears to represent an exaggerated oculogyric crisis, with involvement of the muscles of the jaw and spine presumably through the medium of the extrapyramidal system.

A question of further interest, therefore, is the exact site of induction of this combination of trismus and opisthotonos, and its possible bearing on the unexplained predominance of these features in tetanus.

R. D. MONTGOMERY, M.B., M.R.C.P.,
University College Hospital of the West Indies.
V. L. SUTHERLAND, M.B.,
Kingston, Jamaica.

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Reviews

MECHANISMS OF HYPERTENSION

Mechanisms of Hypertension: With a Consideration of Atherosclerosis. By Henry Alfred Schroeder, M.D., F.A.C.P. (Pp. 379+xv; 67s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1957.

Dr. Schroeder has already given us previous monographs on hypertension. Recent years have shown that the more severe forms of hypertension are yielding to vigorous treatment by antihypertensive drugs. This experience is causing general physicians to take a closer interest in the possibilities of treatment of this disorder. In spite of the simplicity of its recognition, we know relatively little about its aetiology. Dr. Schroeder approaches the aetiological problem as one of considerable complexity, and he discusses the various factors with a very thorough documentation of the literature. Such matters as inheritance and heredity, neurogenic mechanisms, renal mechanisms, and the possible place of trace metals in the aetiology of the disorder are fully discussed. Atherosclerosis is such a constant accompaniment of hypertension after middle life that it gets a chapter to itself, including a discussion of some of the recent theories concerning the role of fat and other lipids in its production. Thereafter the book concludes with some discussion on treatment by modern drugs, including various combinations of drugs.

The whole monograph is one of closely argued reasoning, and the author does not shrink from giving us his own personal views and personal interpretations of the complex mechanisms involved. Time will tell whether or not these are acceptable. No physician interested in the subject can afford not to consult this monograph. He will find in it many views and opinions which may be novel, complex, and even highly speculative, but we must admire Dr. Schroeder for the courage with which he is prepared to put forward hypotheses. A courageous attempt at synthesis of some of the available information is ultimately more helpful to progress of our understanding than a defeatist attitude based on confusion. The book will be a valuable contribution to the ultimate understanding of a complex and highly important medical problem.

J. MCMICHAEL.

LIFE INSURANCE MEDICINE IN THE U.S.A.

Life Insurance and Medicine: The Prognosis and Underwriting of Disease. Edited by Harry E. Ungerleider, M.D., F.A.C.P., and Richard S. Gubner, M.D., F.A.C.P. (Pp. 994 +xviii; illustrated. £6 5s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1958.

This book is derived from a series of lectures given under the auspices of the Board of Life Insurance Medicine in the U.S.A., presumably to actual or potential "medical directors" of life assurance companies and lay underwriters. It is a postgraduate course in the "Specialty of Life Insurance Medicine" by 54 contributors, actuaries and physicians. There are four sections—on "Fundamentals of Life Insurance," "Non-medical Aspects," "Medical Aspects," and "Accident and Health Insurance."

The general insurance principles set out in the first two parts apply with equal force in Great Britain as in the United States, but many of the techniques used to solve the problems do not. Since these techniques are sometimes interwoven with the principles, the going for the British reader is often heavy. Many British readers will be interested in the principles and application of the Numerical Rating System widely used in the American life offices. In these sections there is much overlapping between chapters and no little inconsistency as between authors—a feature which is permissible, even desirable, in a series of lectures, but a blemish in a textbook. The section on "Medical Aspects" occupies more than half of the book and almost constitutes a textbook on internal medicine. There are several admirable chapters, notably those on blood pressure, overweight, and peptic ulcer, in which the respective authors, keeping themselves within their terms of reference, have discussed with full statistical data the mortality significance of these very common impairments. In others of the medical chapters, however, the authors stray into clinical medicine and even therapeutics, failing to make very effective contributions to these subjects and often failing, chiefly for lack of the necessary statistical information, to offer the firm prognostic information which the editors in their introduction lead the reader to expect.

The collection of a series of lectures within the static covers of a book requires stronger and more ruthless editing than this book has enjoyed. While some chapters are a joy to read, the writing is for the most part undistinguished and some of it is very bad. Surely it should be possible for authors, and editors, at least to agree on whether "data" should be treated as a singular or a plural noun, even if they are wrong. The book is finely produced with handsome type on good paper, but it weighs 4 pounds avoirdupois.

J. G. M. HAMILTON.

SEX FOR THE ADOLESCENT

He and She. By Kenneth C. Barnes. (Pp. 207; illustrated. 10s. 6d.) London: Darwen Finlayson. 1958.

Drawing on his experience as headmaster of a co-educational boarding-school, and being assisted by his wife and his medically qualified daughter, Mr. Barnes has produced one of the best of the many books designed to educate the adolescent in sex which I have read. It gives the necessary information on sex anatomy and physiology, and tackles with courage and without the mincing of words many matters of detail which for ever raise questions in the mind of youth but which are so often side-stepped by generalizations and stereotyped phrases.

The author concentrates on rationalizing those codes of conduct laid down by society against which it is natural for the adolescent to wish to rebel. The easy arguments put forward to justify departures from the accepted conventions are taken up and answered. The overpowering strength of the sex urge, and the consequent ease with which any member of the community can lose self-respect and the respect of a heterosexual friend, is emphasized. Therefore, the writer argues, relations between youthful individuals of opposite sex should be based on common intellectual interests and pastimes, and physical contacts which might lead to uncontrollable impulses should be deliberately and consciously avoided.

Mr. Barnes largely succeeds in not giving the impression of preaching. Rather does he map out situations which raise questions, leaving the reader—whom he treats as an adult—to answer them. His book

is intended for schoolboys and undergraduates, but to me seems equally appropriate for girls, and even for parents. I lent it to a sixth-former, just past his 18th birthday, to read. His only comment was: "It's all right for boys, but not for young men." This typical teenage reaction will not surprise Mr. Barnes, but it does indicate the difficulty which confronts all those who would guide modern youth, and emphasizes the need to start the guidance at an early age.

T. N. A. JEFFCOATE.

DRUGS AND THE MIND

Drugs and the Mind. By Dr. Robert S. deRopp. (Pp. 310 +x; 18s.) London: Victor Gollancz, Ltd. 1958.

This book deals with a fascinating topic. It describes all the various ways in which the mind and spirit of man can be got at and influenced by chemical means. A wide ground is covered. The possible chemical causes and theories of madness, for instance, are fully discussed. The new physical treatments in psychiatry are also gone over, and drug addictions are given a special chapter. Naturally, the new chemical tranquillizing drugs get plenty of mention. Another fascinating part of the book is devoted to all those drugs which have been used throughout centuries by man to seek temporary relief from grim reality and to create artificial states of euphoria. Some very interesting quotations from eminent writers are given describing their effects. And the author also does not forget to discuss the very large part played by drugs in so many religions to induce states of supposed "possession" by gods, and so greatly enhance feelings of religious certainty and belief.

But there are drawbacks to this book. It is popularly written for lay consumption, and it is not written by a medical man, but a Ph.D. A large amount of the medical material included therefore consists of quotations and abstracts from papers in medical journals and from medical books. The author's obvious ignorance of some of the medical matters he discusses in an often authoritarian manner results in his having to rely on other people's medical judgments, without always being able to assess the real value of what he is quoting. Thus, his highly coloured description of such things as leucotomy can sometimes be damagingly misleading. A layman may easily get some quite wrong viewpoints about various matters discussed in the book. This work, however, can be useful to doctors wanting further information about these interesting topics, for they can much better keep their tongues in their cheeks and sense where the desire for dramatic effects has overlaid strictly factual reporting.

WILLIAM SARGANT.

Monograph No. 5 of the Physiological Society is an account of *The Mammalian Cerebral Cortex*, by Professor B. Delisle Burns, of McGill University (pp. 119, illustrated; Edward Arnold, Ltd., 21s.). The author has, so far as possible, avoided the use of terminology particular to neurophysiology, making the book more easily digestible by the scientist and general reader. It contains a number of illustrations and a useful bibliography.

For the fifth edition of *Modern Clinical Psychiatry* Dr. A. P. Noyes has had the assistance of Professor L. C. Kolb, of Columbia University. Besides a general revision of the text there is a new chapter on the legal aspects of psychiatry in the United States. The book is published by W. B. Saunders Company (694 pages; 56s.).

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Die Pränatalen Infektionen des Menschen. Unter Besonderer Berücksichtigung von Pathogenese und Immunologie. By H. Flamm. (Pp. 135+xi; illustrated. DM. 19.80.) Stuttgart: Georg Thieme Verlag. 1959.

Physiologie des Bewusstseins in Entwicklungsgeschichtlicher Betrachtung. By U. Ebbecke. (Pp. 211+xi; illustrated. DM. 27.) Stuttgart: Georg Thieme Verlag. 1959.

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STAPHYLOCOCCAL INFECTIONS IN HOSPITALS

A subcommittee of the Standing Medical Advisory Committee of the Central Health Services Council has issued a report[1] entitled "Staphylococcal Infections in Hospitals" which defines what is now generally recognized to be a very serious problem[2] and makes proposals for dealing with it. The first step is "ascertainment." It is astonishing but true that the staffs of hospitals or units where systematic records of infection are not kept deny that it presents any problem, although subsequent investigation may show a clean-wound infection rate of 5% or more. The report suggests that this record be kept by the ward sister, and reviewed by a "control of infection officer," a senior member of the staff who may well be the hospital bacteriologist, behind whom there is a "control of infection committee." A good point is made in the suggestion that ascertainment involves follow-up: breast abscesses, for example, often develop after discharge from a maternity unit. The laboratory is enjoined to keep cultures of staphylococci in case they may be needed in later epidemiological study. In a section entitled "Sources of Infection and Modes of Spread" a distinction is drawn between a source of infection in the sense of a septic lesion in which bacteria are multiplying and a "depot" such as dust or contaminated utensils in or on which they merely survive: apparently reference to dust as a source of infection has given rise to the idea that staphylococci actually proliferate in it.

The first of seven "principles of prevention" laid down is the "provision of adequate accommodation and staff," and in many hospitals it is to be feared that this initial requirement will prove an obstacle to fulfilling most of the remainder. It is rightly emphasized that all infected cases should be isolated, and the figure of 20% is mentioned as the proportion of beds which should be isolation beds. But how many hospitals have so many? The dressing of wounds only "in properly designed treatment rooms" is admittedly put forward only as an ideal, but when it is enjoined that not only the cleaning of floors but the drawing of bedside curtains should be completed at least 15 minutes before dressings begin in a ward, the report seems to be admitting a risk without suggesting a feasible remedy for it. These curtains have been shown to harbour staphylococci, and they are used to screen patients for dressings: a staff which could be depended on to immobilize them so as to fulfil this requirement would need to be working in a very leisurely way. Some other rather impracticable suggestions are made: "Theatre units should be provided with showers or baths," and "ideally every member of the surgical and nursing team should bathe before each operating session," although it is admitted that this may not "often" be possible. Movement of persons in the operating theatre should be limited: "a nurse crossing the room raises a cloud of airborne organisms and some of these may land in the wound or on sterile equipment"; and the provision of seats to encourage immobility on the part of nurses and orderlies is suggested. The picture evoked by this recommendation seems rather far from reality.

Another difficulty which may be met in attempting to carry out these recommendations is that they will demand facilities for the phage-typing of staphylococci on an unprecedented scale. Without such information epidemiological study is working in the dark. Since phage-typing will presumably not always be possible, it might have been emphasized that the more dangerous types of staphylococcus are often resistant to several of the major antibiotics, including tetracycline, and the pattern of antibiotic resistance, which any laboratory can ascertain, is therefore an alternative if less precise method of classification.

Sensible rules are proposed for restricting the use of antibiotics, including a limitation of authority to prescribe some of them to the senior staff, and a general warning against non-specific prophylactic use. The treatment of nasal carriers by antibiotic or antiseptic applications is advocated only in the presence of an outbreak.

The report gives detailed instructions for many nursing procedures, including isolation nursing. Nearly all of these entail the wearing of gowns, gloves, and masks, "or other protective clothing," and it seems that a nurse's face or uniform will not often be seen. In this connexion it is mentioned that "the usefulness of masks in maternity services (other than premature babies' nurseries) is equivocal": this statement may possibly be based on findings published in this *Journal* by J. O. Forfar and A. F. Maccabe,[3] although this paper is not in the reference

[1] Ministry of Health, Central Health Services Council, Standing Medical Advisory Committee. *Staphylococcal Infections in Hospitals—Report of the Subcommittee*. 1959. H.M.S.O., London. Price 2s. 6d. net.
[2] See leading article, *Brit. med. J.*, 1958, 1, 207.
[3] Forfar, J. O., and Maccabe, A. F., *ibid.*, 1958, 2, 76.

list of the report. These authors did indeed find that there was no more sepsis in a maternity unit when the use of both gowns and masks was much reduced; and maternity and surgical work are not so fundamentally different that this finding need be altogether disregarded in other fields. If the lavish use of protective coverings could be curtailed a great deal of time and money would be saved. It is even conceivable that if masks were worn less and the noses of the staff were thus naturally ventilated fewer would become carriers and sepsis might consequently diminish.

The reader is referred to other publications for advice on sterilization and disinfection. Sterilization by heat is now engaging much attention in other quarters, but some rather more specific advice about chemical disinfection would have been helpful, both as it concerns the surgeon's or the patient's skin and for some of the 25 varieties of inanimate objects mentioned in paragraph 83 as capable of acting as depots for staphylococci.

There is very little that is original in this report: it gives instructions at length—and with careful definition of the duties of each member of the staff ("The matron should ensure adequate training and supervision of nursing staff . . .")—for precautions against cross-infection, most of which in some form are now standard practice so far as facilities permit. It offers no hope that this is a problem which further research may greatly simplify. If staphylococci were luminous and we could watch their migration, it might prove that some of their modes of spread are of little account, and that much more good could be done by concentrating on a few items of technique involving special risk. It is most fervently to be hoped that this subject will be further clarified by studies now in progress. A tedious and costly prospect awaits us if the full instructions given here have to be permanently incorporated in hospital practice throughout the country.

DIABETES IN THE TROPICS

Diabetes seems to be relatively mild among peoples of the tropics. Their illiteracy and poverty often make dietary control and insulin treatment difficult or erratic, yet ketosis and diabetic coma are rare. This lack of ketosis is especially surprising in children or young adults, for experience in Europe or North America is that when diabetes starts early in life it is severe in that the patient must have regular insulin to prevent ketosis.

In temperate regions most diabetics belong to one of two types[1]—those (type 1) whose diabetes starts early and who need insulin, and those (type 2) whose disease comes on in middle age, who tend to be obese, and whose diabetes is often readily controlled simply by restricting diet and who seldom need insulin except when they acquire infection. Although these two types are not always clear-cut, the evidence is in favour of two main causes of diabetes.[2] In type 1 the pancreatic β-cells are damaged and produce little insulin, and so in these patients insulin is essential to replace the lack, though they seldom require more than about 50 units daily. They are sensitive to insulin and readily develop hypoglycaemia if it is given very little in excess of their needs. By contrast, in type 2 diabetes, the β-cells are normal and produce a great deal of insulin, so that these patients are insensitive to more, yet they are diabetic probably because of the presence of a substance interfering with insulin action—a substance believed to be elaborated by the pituitary.

In 1955 P. Hugh-Jones[3] studied diabetes in Jamaica and found there, as in Britain, an excess of female patients with characteristic type 2 diabetes. Type 1 diabetes was relatively uncommon, and there was a third variety, not previously described, which occurred about half as often as the usual type 1 cases. This third variety (which he called type J), like type 1, started in young persons or even children, who were underweight, but, unlike type 1 patients, were insensitive to insulin and often required over 100 or more units daily to control their glycosuria: moreover, they did not readily develop signs of ketosis if these large doses of insulin were withdrawn. Besides this unusual type J, he noted, as had previously been observed in Jamaica, some examples of apparently temporary diabetes in young persons. These peculiarities in diabetes in Jamaica have since been confirmed there, reports have been received of similar findings elsewhere in the tropics, and now in this issue of the *Journal* Dr. J. E. Cosnett reports similar findings among the Indian population of Natal.

The fact that Dr. Cosnett has found these unusual characteristics of diabetes among the Indian population rather than among the Negro races is worthy of note. In a previous article[4] on illness among Natal Indians he had shown that they were admitted to medical wards more often because of diabetes than any other single disease, whereas the admissions of the Bantu Negroes for diabetes were

[1] Lawrence, R. D., *Brit. med. J.*, 1951, **1**, 373.
[2] Graham, G., ibid., 1940, **2**, 479.
[3] Hugh-Jones, P., *Lancet*, 1955, **2**, 891.
[4] Cosnett, J. E., *S. Afr. med. J.*, 1957, **31**, 1109.
[5] Pyke, D. A., *Lancet*, 1956, **1**, 818.
[6] Hugh-Jones, P., and Pyke, D. A., *Proc. 3rd Congress Int. Diabetes Fed.* (to be published).
[7] Wright, H. B., and Taylor, B., *W. Indian med. J.*, 1958, **7**, 123.
[8] Himsworth, H. P., *Lancet*, 1949, **1**, 465.

very low. Despite the danger of a sampling error when hospital admissions are used to assess the frequency of disease in a population, there seems little doubt that in South Africa the Indian population is much more susceptible to diabetes than the Negro, and that diabetes occurs there in the same characteristic forms as it does in Jamaica and elsewhere in the tropics.

Study of the nature of diabetes in the tropics should contribute to a better understanding of the mechanism of the diabetic syndrome. Although the nature of type 1 diabetes, but not its cause, seems clear, the nature of type 2 is still a matter for speculation. It is generally held that obesity is the main factor in producing type 2 diabetes: an abnormal glucose tolerance curve in a type-2 diabetic may be restored to normal after the patient loses weight. D. A. Pyke,[5] however, has put forward evidence that, so far as women are concerned, it is parity rather than obesity which is the main factor; this would account for the great preponderance of females in diabetics over 45 years old. In Jamaicans and Natal Indians the same explanation may hold, but in some parts of Africa, India, China, and Japan men with diabetes appear to outnumber women.[6] It may be that men are more often selected for hospital treatment than women, though competent observers are not satisfied that this is the reason for the anomaly.

More work is needed to explain the other differences between diabetes in tropical and temperate climates. Hospital investigations might show, for example, whether or not type J diabetics lack insulin in the plasma, and it is plainly of importance to establish whether it is racial, dietary, or other environmental factors which determine the frequency and type of diabetes. The evidence of Dr. Cosnett that the incidence of diabetes in Natal Indians is more than would be expected in a mixed community is confirmed by a study of a sample of diabetics among mixed Indian and Negro races in Trinidad.[7] The unusual types of diabetes seem to occur in both these races in a tropical or subtropical environment, though type J has not been reported in Europeans in the tropics.

Now that it is easy to detect glycosuria by dipping test-papers into urine, it should be practicable to measure the prevalence of diabetes and its distribution according to age and sex—assuming glycosuria is a measure of diabetes in health surveys—in different communities in the tropics. The results might well lead to a better understanding of the disorder, for, as Sir Harold Himsworth has said,[8] "a primary deficiency of insulin is only one, and then not the commonest cause of the diabetic syndrome."

CATCHING UP WITH CABOT

Forty-nine years ago Richard Cabot held the first of a series of weekly clinicopathological exercises, as he named them, at the Massachusetts General Hospital. They were intended for the hospital's house officers and medical visitors. This was the start of the series which later won world renown through their publication in the *Boston Medical and Surgical Journal* (now the *New England Journal of Medicine*) as the "Case Records of the Massachusetts General Hospital." The series has continued uninterrupted to this day, a notable record. Cabot died on May 8, 1939, and three days later, at the next clinicopathological conference, Dr. Mallory,[1] his successor as their editor, opened the proceedings with a tribute to him. He quoted from a letter Cabot had recently written to Dr. Washburn for the latter's history[2] of the hospital, telling how the conferences started. "At the beginning of 1910," wrote Cabot, "I began, on my own initiative, to hold exercises with the house officers and medical visitors to the hospital—a weekly exercise in connexion with Dr. J. Homer Wright, modelled essentially like the later clinicopathological conferences." Before then, it is true, Cabot had been in the habit of holding case conferences with his students, but in these there was no association with the pathologist and no demonstration of post-mortem results—the twin hallmarks of his later conferences. It was the finding in the records of the Massachusetts General Hospital of a case still labelled "neurasthenia," despite necropsy evidence of cancer of the pleura, which finally impressed upon Cabot the need for confronting the clinician with the lessons of the post-mortem room. This was what really started the series. At first Cabot published his case histories, mostly with post-mortem details, in book form.[3 4] In 1915, however, his secretary began recording the discussions also, and these were included in the material circulated, with the clinical and post-mortem reports, to a restricted list of physicians. Later still came publication in the *Boston Medical and Surgical Journal* and the *New England Journal of Medicine*.

This week, following Cabot's pioneering footsteps, we report (p. 224) a clinicopathological conference held at the Postgraduate Medical School of London, at which Professor Robert Platt, P.R.C.P., was the guest speaker. It is the first of a series of such reports, of which we hope to publish some eight to ten a year to begin with. Much of the educational value of

[1] *New Engl. J. Med.*, 1939, **220**, 880.
[2] Washburn, F. A., *The Massachusetts General Hospital*, 1939, Houghton Mifflin Co., Boston.
[3] Cabot, R. C., *Differential Diagnosis*, 1911, Vol. I, W. B. Saunders, Philadelphia.
[4] —— ibid., 1914, Vol. II, W. B. Saunders, Philadelphia.

these conferences depends, as Dr. Alan Gregg pointed out long ago,[1] on the candour and fearlessness of the participants. The clinician, and for that matter also the laboratory worker, who in discussion is prepared to chance his arm, confess ignorance, or air a doubt gives a wholesome example to his colleagues.

The *New England Journal of Medicine* has long set us an example, not least in publishing the "Weekly Clinicopathological Exercises." If we have been slow in catching up with Cabot, it is perhaps because of the embarrassing clinical wealth of London's many teaching hospitals. But the Postgraduate Medical School at Hammersmith stands apart, is fertile in research and experiment, and, with its exceptionally able staff, has generously agreed to try with us to follow the example of our New England colleagues in Boston.

AMBLYOPIA

That amblyopia is a serious problem has been known for a long time, and much study and research have been devoted to it. But Mr. R. B. Wellesley Cole's findings, reported elsewhere in this issue (p. 202), will come as a surprise to many: he found amblyopia present in 53 out of every 1,000 patients examined by him under the supplementary ophthalmic service of the National Health Service. Probably more than half of these could have been cured if only the disorder had been recognized in early childhood.

The recognition and subsequent treatment of amblyopia in young children are both processes which tax the knowledge and experience of the examiner. Amblyopia can be defined as the inhibition of retinal response in one eye, which as a consequence may become nearly blind. Under the present system of sight-testing at schools it is hardly surprising that numerous cases of amblyopia remain unnoticed. If the examination and treatment of all children with suspected defects of vision were carried out under skilled medical supervision, much of the wastage of good sight caused by amblyopia could be prevented and affected children would have a better chance of possessing two useful eyes working together instead of just one effective eye.

To have one blind eye is sometimes not an apparent handicap, since it is occasionally found at routine examination of patients who ask for reading-glasses about the age of 40. But the higher the intelligence of the patient and the more skilled his occupation, so much the greater is likely to be the disadvantage of having a nearly blind eye and of lacking stereoscopic vision. There are degrees of amblyopia, some being very severe, rendering the eye almost incapable of useful vision, while others may just entail a reduced visual acuity for detail. As Mr. Wellesley Cole notes, the earlier the age of onset, say before 6 months, the more severe the defect. It is thought that the defect is a cortical inhibition: it affects form vision primarily, but not the perception of light or its location. It is for this reason that an amblyopic eye often goes unnoticed. The fundus is always found to be normal.

The causes are refractive errors, either hypermetropia or high astigmatism, squint, cataract, and idiopathic. Treatment is by correction of refractive errors, occlusion of the good eye, and orthoptic exercises and training.

The examination of young children demands patience, understanding, and time, and if amblyopia is to be prevented it is essential to examine children for it at an early age. There are useful picture charts which enable children under the age of 4 to be tested with reasonable exactness, and the E-test, with this letter pointing in four different ways, is soon mastered and is an even better indication of visual acuity. The method used in the E-test is to cut out a cardboard E for the child to hold, and, while one eye is properly occluded by the parent, the examiner points to each letter in turn and observes how the child manipulates the E. The age at which a child can usefully do one of these tests varies between 2 and 4. If a difference of two or more lines of the chart exists between each eye, then amblyopia almost certainly exists. There are suitable tests for even younger children, or a trial of occlusion can be made if amblyopia is suspected because of intermittent squint or family history. Mr. Wellesley Cole stresses the strong element of heredity in this disorder.

Prevention of amblyopia depends greatly on the appreciation by the medical profession and the public of the magnitude of the disability and the numbers of people affected. Medical students often say that ophthalmology is a closed book to them, and many of them are content to leave it at that, even after qualification. The teaching of ophthalmology in the medical schools is for the most part unsatisfactory. Usually so little time is allotted to this subject in the curriculum that nothing but the elements of examination, ocular physiology, and the broad principles of disease can be taught. Seldom can the nature of so complicated a disorder as amblyopia be discussed and explained: usually the nearest approach to the subject is the merest outline of the two basic types of squint. In drawing attention to the size of the problem Mr. Wellesley Cole's report is therefore of great value. As he says, the examination of all young children before they reach school age would be an administrative problem of some magnitude. But if medical concern is strong enough a mass attack on amblyopia is well within the bounds of possibility.

HOW MANY WEEKS IN A YEAR?

The four Registrars-General of the British Isles usually agree on how many weeks they count in a year, but in 1958 they unfortunately failed to do so. Owing to the vagaries of Earth and Moon in their respective orbits, it is sometimes necessary to count 53 weeks, because the usual number of 52 leaves a day and a bit to be added in later. The Registrars-General for England and Wales and for Northern Ireland took up the slack in 1958, giving it 53 weeks, but their colleagues in Scotland and the Irish Republic jumped ahead into 1959—inspired, perhaps, by the new Russian satellite and the Chinese "leap in advance." Consequently, though our Table of Infectious Diseases and Vital Statistics this week is headed week No. 53, that is only the number

that England and Wales and Northern Ireland are giving it; Scotland and the Irish Republic are calling the same week No. 1 of 1959. The discrepancy will continue through 1959, but will presumably be rectified in 1960, for Scotland and the Irish Republic cannot avoid the responsibility of taking the extra days under their wing some time. Provided this numerical discrepancy is kept in mind, no confusion in using the Table need arise, since it also bears the calendar date of the week whose statistics are printed there. And the four parts of the British Isles are still agreed on the date.

DANGEROUS LAXITY

In its latest report the Permanent Central Opium Board[1] describes as an "unfortunate state of affairs" the control of certain drugs of addiction in some European countries. Indeed, the absence of proper control by the Federal Republic of Germany over one of them, normethadone, is described as a "dangerous situation."

Reporting the drug to be no less dangerous than morphine, the Board states that normethadone has been compounded in antitussive preparations marketed under the names "taurocolo" and "ticarda." West Germany is said to be the chief manufacturer of normethadone, and, not being party to an agreement known as the 1948 Protocol, was not bound to bring the drug under national control—"nor has it yet felt moved to do so." A spokesman for that Government has since declared[2] that West Germany would publish a law soon acceding to it. We understand that these cough mixtures have not been imported into Great Britain but that they have in the past appeared in some British Colonies. These include Aden, Cyprus, Gibraltar, Hong Kong, Nigeria, and Singapore.

For about eight months another drug of addiction, dextromoramide, was circulating without full control. A study of its analgesic properties is presented by Mr. E. Cope and Dr. P. O. Jones at p. 211 of the *Journal* this week. Belgium and the Netherlands, the only two countries where this drug is known to be manufactured, delayed in applying full safeguards after being notified in May, 1957, by the Secretary-General of the United Nations that they should do so; each complied in February and March, 1958, respectively. This drug is also known as "R. 875," "jetrium," "palfium," and "pyrrolamidol." The report states that it is "recognized as being more dangerous than morphine." Italy also comes in for criticism in permitting the dispensing of small quantities of acetylmorphine in 1953 and 1956 without medical prescription.

The control of these dangerous drugs obviously needs continuous and vigilant attention. The slightest laxity soon leads to trouble, and it seems to have done so over normethadone, of which the report states: "In the Board's view this situation is such as to cloak a dubious traffic."

[1] *Report to the Economic and Social Council on the Work of the Board in 1958*, 1958. United Nations, Geneva.
[2] *Manchester Guardian*, January 16.

HEALTH OF SCHOOLCHILDREN

The school medical service came into being in 1908,[1] and the latest report[2] of the Chief Medical Officer of the Ministry of Education contains a useful history of its development and a record of what it has achieved in fifty years. In his introduction Sir John Charles gives some illuminating facts:

"Of every 1,000 children medically examined in the early days of the service, 140 were verminous, 130 undernourished, 100 had defective footwear, 50 had inadequate clothing, 40 had rickets, and 30 had heart disease. In 1957, 40 in every 1,000 were verminous, 17 were of unsatisfactory physical condition, 2 had heart disease, none had rickets, and a negligible number had inadequate clothing and footwear (although many had shoes which were too small or too large) . . . In Sheffield . . . the average weight of a 14-year-old boy in a poor district was 27 lb. (12 kg.) more than the average weight of all 14-year-old Sheffield boys in 1920."

The slowness of the decline in the numbers of verminous children is disappointing: about a quarter of a million children were found to have verminous heads in 1957. But in most other respects the handicaps associated with poverty and ignorance are now little in evidence. Many children still suffer from lack of sleep, as they did fifty years ago for different reasons, and it is a reflection on the good sense of modern parents that 30% of the boys and 15% of the girls in a secondary modern school in the Isle of Wight were, in 1957, "regular smokers." The eating of sweets, iced lollies, biscuits, and carbohydrate foods in excessive quantities is said to be the main cause of obesity in children, which is now attracting at least as much attention as undernutrition.

The disorders for which children are now admitted to special schools are for the most part very different from those of 50 years ago, though blindness and deafness still loom large among them. The report states:

"It is little short of miraculous that in the brief space of two generations many of the diseases which destroyed or crippled children have passed, or appear to be on the point of passing, into epidemiological history so that the remaining causes of crippling, and, indeed, of some other handicaps of children, are now mainly congenital or hereditary in origin."

In the section of the report concerned with the medical inspection and treatment of schoolchildren the warning is given that osteochondritis of the spine may sometimes arise from the vigorous performance of exercises prescribed for "poor posture." In general, about 15% of children entering school are found to have defects (excluding dental disease or infestation) requiring treatment, and it seems from inquiries made in two areas that about half of these children were not receiving the treatment they needed.

Among the report's 21 chapters on various aspects of the work of the school health service there are particularly informative ones on accidents in childhood and on tuberculosis in the schools. One school medical officer quoted in the report is right to emphasize that tuberculosis in children is still relatively common. But

[1] See leading article, *Brit. med. J.*, 1958, **1**, 633.
[2] *The Health of the School Child—Fifty Years of the School Health Service—Report of the Chief Medical Officer of the Ministry of Education for the Years 1956 and 1957*, 1958. H.M.S.O., London. Price 10s. 6d. net.

the very real achievements of the preventive medical services can be seen from figures like these: in 1912 there were in Manchester's residential school for cripples 73 children with tuberculosis of the spine, hip, or knee; now there are no children with such infections in the city's residential school, though there are still 20 children with surgical tuberculosis attending the special day school.

TREATMENT OF MEASLES

The chances are that this will be a "measles year," for the incidence tends to be high every other year in Great Britain, and an outbreak is now due. As the graph in our Vital Statistics section shows (p. 244), the weekly totals of notifications in England and Wales have risen sharply to about 18,000. To the normal healthy child uncomplicated measles carries little risk. When the child is already debilitated or when complications occur, it can be a serious and even dangerous disease. It is therefore specially desirable to prevent the disease attacking ailing or very young children.

Gamma globulin given to a child contact of measles at the correct time and in the correct dose will usually modify or prevent the disease.[1] It is worth remembering that 9 ml. of gamma globulin is roughly the yield of 1 pint (0.6 l.) of blood, so that economy in its use is essential. The severe complications of measles are commonest in children under 3 years of age, and, unless there are special reasons, gamma globulin should not be given to older children. Measles is not usually diagnosed before the first or second day of the rash, so that contacts have been exposed for four or five days to infection: 3 ml. gamma globulin given to a child under 3 years is more likely at this stage to modify than to prevent an attack. Given in the first two days of exposure, this dose will probably prevent an attack; but, for home contacts, modification is better policy, because it results in permanent immunity. For older children the dose may be increased to 6 ml. or 9 ml. for prevention, but 3 ml. will still often produce modification.

The main complications of measles are acute respiratory infections and otitis media. Though sulphonamides or antibiotics are sometimes prescribed in the hope of preventing these complications, it is not certain that they do so. A report of the College of General Practitioners[2] claimed that the routine use of sulphonamides in measles increased the total number of complications, though it reduced the incidence of otitis media in children with a past history of ear infection. Penicillin seemed to have some effect in reducing pulmonary complications, but the routine use of antibiotics was considered largely unnecessary.

The treatment of complications when they have occurred is another matter. Otitis media will nearly always respond to sulphonamides or penicillin, and acute mastoiditis is now rarely seen after measles. Pulmonary complications are usually due to secondary invasion with haemolytic streptococci or pneumococci, organisms which are almost invariably sensitive to penicillin. In fact, before any other antibiotic is given examination of sputum should ideally first have shown that the predominant organism is not sensitive to penicillin. The first one or two doses of penicillin in an ill child are best given by injection in a dose of 100,000 units every four hours. Thereafter a therapeutic level in the serum can be obtained by giving penicillin by mouth in a dose of 200,000 to 400,000 units every four hours. Full supportive treatment with oxygen if necessary would also be given. If this treatment is reserved for patients with signs of respiratory complications, and not given as a routine to all patients simply because they have a raised temperature and a cough, the mortality from measles should be negligible and much penicillin will have been saved. If it can be arranged, an *x*-ray examination of the chest should be carried out after any pulmonary complication. Though residual changes may sometimes be seen, permanent lung damage after measles is now rare.[3]

[1] *Brit. med. J.*, 1954, **2**, 1093.
[2] College of General Practitioners, *Research News Letters*, No. XI, 1956, and No. XIV, 1957.
[3] Fawcett, J., and Parry, H. E., *Brit. J. Radiol.*, 1957, **30**, 76.

PROTON-BEAM THERAPY

According to reports[1] in several newspapers Professor L. Leksell and his colleagues at Uppsala have destroyed a small area of tissue in a patient's brain by directing upon it a beam of protons from a synchro-cyclotron, thus successfully relieving the patient's symptoms. These workers have recently described their experimental work,[2] but so far no details of their clinical use of the synchrocyclotron have been reported in medical or scientific journals. It may be assumed that elaborate stereotaxic methods were used to locate the lesion.[3]

Protons, unlike electrons and *x* rays, are not widely scattered in the tissues, and, since they give up their energy when they reach the target, their effects can be narrowly limited to a selected area of tissue.[4] The production of a beam of protons with sufficient energy (of several hundred million volts) to destroy tissue in the brain necessitates the use of apparatus which is scarce, expensive, and used by physicists for a variety of research purposes. The modification of a synchro-cyclotron for medical purposes is quite feasible, but in the present state of knowledge it would be impracticable to use such apparatus solely for therapeutic purposes. There are two synchrocyclotrons in Britain—one at Harwell and one at the University of Liverpool. Workers at the University of California at Berkeley have carried out experimental work on mice, rats, and dogs with the synchrocyclotron there, and have reported on its use to destroy the pituitary gland as part of the treatment of carcinoma of the breast.[5,6] It seems unlikely that proton-beam therapy will have much application in the direct treatment of tumours: what recent work shows is that it can destroy very small areas of tissue capable of being accurately located, in the brain or elsewhere.

[1] *The Times*, January 19.
[2] Lawson, B., *et al.*, *Nature (Lond.)*, 1958, **182**, 1222.
[3] See annotation, *Brit. med. J.*, 1957, **1**, 333.
[4] See leading article, ibid., 1956, **1**, 99.
[5] Lawrence, J. H., *Cancer*, 1957, **10**, 795.
[6] Tobias, C. A., *et al.*, *Cancer Res.*, 1958, **18**, 121.

Clinicopathological Conference

A CASE OF MANY LESIONS

DEMONSTRATED AT THE

POSTGRADUATE MEDICAL SCHOOL OF LONDON

This is the case of a young woman who presented with a multiple arthritis and hypertension (Case No. 194,520; P.M. No. 8,274).

Clinical History

Dr. P. S. KINCAID-SMITH: This patient, a 30-year-old unmarried shop assistant, was admitted as an emergency in November, 1956, complaining of headaches of increasing severity for 3–4 months, blurring of vision for 8 weeks, morning vomiting for 6 weeks, and nocturnal dyspnoea every night for the past two weeks. Rheumatoid arthritis involving many joints had been diagnosed nine years previously, and for this she had been given phenylbutazone. She was very ill, pale, and dyspnoeic at rest: acute pulmonary oedema developed during the examination. There were rheumatoid-like deformities of many joints, including the distal interphalangeal joints, purpura on the limbs, deep blue linear haemorrhagic lesions of the nail-fold, and small depressed scars of the pulp of many fingers. The fundi showed bilateral papilloedema with extensive retinitis. The pulse was 120 and regular, and the blood pressure 250/130 mm. Hg; there was pitting oedema of the ankles and sacrum, 5 cm. elevation of the jugular venous pressure, hepatomegaly, and abundant crepitations throughout both lungs. The apex beat was in the fifth intercostal space just outside the mid-clavicular line and had a left ventricular heaving character. There was a loud atrial sound and third sound, a grade IV regurgitant systolic murmur at the apex, and a short rumbling mid-diastolic apical murmur. The cranial nerves were normal, but there was bilateral exaggeration of the tendon reflexes, increased tone, and bilateral ankle clonus. There was some left-sided weakness and an extensor plantar response on the left. The spleen was enlarged to three fingers below the right costal margin.

INVESTIGATIONS

Renal.—Urine: heavy proteinuria (200 mg./100 ml.), low fixed specific gravity, and many leucocytes and erythrocytes and some casts in the deposit. Blood urea 60 mg./100 ml. Serum proteins: albumin 2.5 g./100 ml., globulin 3.3 g./100 ml., with a non-specific abnormality in the electrophoretic pattern. Renal biopsy showed patchy glomerular scarring, which could have resulted from either malignant hypertension or disseminated lupus erythematosus, but as some glomeruli appeared normal the former cause seemed more likely.

Haematological.—Haemoglobin 8.8 g./100 ml. (60%); M.C.H.C. 31%; reticulocytes 6.7%; W.B.C. 9,000 (82% polymorphs); platelets 280,000. Lupus erythematosus cells were demonstrated with ease on three occasions. Coagulation studies showed an anti-prothrombin type of circulatory anticoagulant. The differential agglutination titre was within the normal range; sedimentation rate 50 mm./hour.

Cardiovascular.—Chest radiograph showed slight left ventricular enlargement with pulmonary congestion. The electrocardiogram indicated left ventricular enlargement.

Skeletal.—Radiographs of the hands showed articular erosions of the carpal and metacarpal bones.

SUBSEQUENT COURSE

The patient was started on hypotensive treatment (initially parenteral pentolinium; later oral mecamylamine) and prednisone, 20 mg. four times daily. There was an excellent clinical response. However, while on this treatment she had further neurological episodes, developing marked weakness and pyramidal signs first on one side and then on the other. The cardiovascular signs fluctuated, but their general trend was towards improvement and the disappearance of the added sounds and murmurs; one month after the start of treatment there was clinical and electrocardiographic evidence of a pericarditis. In February, 1957, she was discharged ambulant on hypotensive treatment and prednisone, the dosage of prednisone having been reduced to 15 mg. three times a day. The papilloedema had resolved completely a month after her discharge and the retinitis after another two months.

She remained moderately well until May 10, 1957, when she was readmitted because of increasing weakness and the development of a tremor which was ascribed to the mecamylamine, as it disappeared when the drug was withdrawn. The sedimentation rate had risen from 4 mm. the previous month to 100 mm., and a chest radiograph revealed a small infraclavicular shadow on the right. Numerous specimens of sputum and gastric washings were negative for acid-fast bacilli. However, by June 11 an apical lesion had appeared on the right (Fig. 1). Further attempts to isolate the tubercle bacillus failed until July 30, when it was found in two gastric lavage specimens. Anti-tuberculous treatment with streptomycin and ioniazid was started at this time, the dosage of streptomycin being later reduced. Chloroquine was also given, but was stopped after 8 weeks because of the development of muscle weakness. Over the next few months her general condition improved. The blood urea remained stable at 80 mg./100 ml., and the proteinuria diminished considerably, being absent from several 24-hour specimens in early October. Thereafter, however, she gradually deteriorated for no very clear reason. The blood pressure was controlled and the sedimentation rate remained low, but she developed extreme muscle weakness which progressed and was the major symptom in a downhill course until her death on January 11, 1958.

GUEST SPEAKER: PROFESSOR PLATT

Professor ROBERT PLATT: This is a case in which I don't suppose anybody has any doubts at all about the diagnosis. I should have thought the diagnosis was so clear on clinical grounds that if the pathologists have not

found the specific changes it is because they have been obscured by superimposed malignant hypertension. There are, on the other hand, many very interesting features of the case on which one can comment.

In the first place, why is the diagnosis so abundantly clear? From the very beginning there were some interesting and suspicious features. This woman had rheumatoid arthritis or polyarthritis of rheumatoid appearance and type for nine years. Now when that is followed later by the development of severe hypertension I would say that it leads you straight away to a diagnosis of collagen disease of the disseminated lupus or periarteritis type. Those are the only two conditions in which I have seen "rheumatoid arthritis" in an illness which later leads to severe hypertension. Severe hypertension is of course much commoner as a complication of periarteritis nodosa than it is of disseminated lupus, but we have seen it plenty of times with disseminated lupus.

Now, another thing is that the rheumatoid arthritis was in this case accompanied by a negative sheep-cell or differential agglutination test, and I think that the experts would immediately say that this is probably not ordinary rheumatoid arthritis for that reason alone and that it is much more likely to be in the group of disseminated lupus. Of course, where borderlines are to be drawn between these various types of collagen disease (including rheumatoid itself) is a very big subject on which I certainly wouldn't like to comment. Next she develops four major symptoms which are quite clearly the symptoms of malignant hypertension—they can't really be anything else. The first three could be symptoms of cerebral tumour, but not when accompanied by the fourth—namely, nocturnal dyspnoea—and when you link that up with a characteristic retinopathy and with a diastolic pressure of 130—I am only surprised that it wasn't even higher—then your diagnosis of the malignant phase of hypertension is very obvious. So I propose now to go through the case quite briefly, picking out some of the features just to comment on them and to test their appropriateness to the diagnosis of malignant hypertension, secondary to the renal lesion of disseminated lupus.

She had a skin lesion which I can get out of commenting on by saying that I didn't see it; but of course, as you know, these cases of lupus don't all show the characteristic skin lesions. They very often get the finger lesions, the erythema of the fingertips and round the nail, so often followed by ulceration, which no doubt was the cause of the scars on her fingers. In addition to her polyarthritis, of the usual kind, she had limitation of movement of the spine, especially the cervical spine, which of course can be seen as a feature of both classical

FIG. 1.—Mitral valve showing vegetations on auricular surface and thickened chordae tendineae.

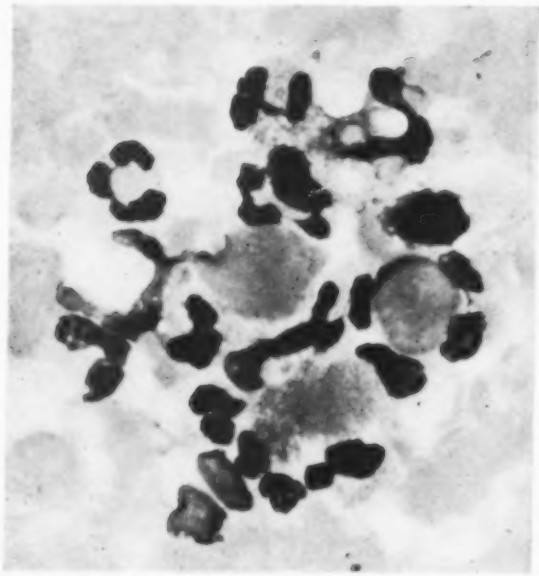

FIG. 2.—Typical L.E. cells (×1,000) showing phagocytosed and free masses of degenerate nuclear material with loss of chromatin pattern.

rheumatoid arthritis and also the arthritis of disseminated lupus, so there is nothing difficult there from the point of view of diagnosis.

The purpura is interesting. The platelet count was 280,000. Quite a number of cases of disseminated lupus start as a purpuric illness, and many of them are thrombocytopenic, but not by any means all of them—in quite a number of these patients the spleen has been removed on the assumption that they are cases of primary thrombocytopenic purpura, and only later do they develop other lesions of disseminated lupus. There is, however, the very interesting finding of a circulating anticoagulant, which I will deal with later.

There are a number of cardiovascular findings which could be, I think, and perhaps must be, interpreted as evidence of the Libman–Sacks type of endocarditis which occurs in disseminated lupus. Though I am not an expert cardiologist I don't think these could be simply explained away as secondary to cardiac dilatation from her hypertensive state. She also had lesions in the nervous system, of which we heard more later on when new lesions occurred, which I should have thought unquestionably were due to minor infarcts in various parts of the brain, and therefore I would forecast that such infarcts would be found at necropsy, probably secondary to fibrinoid lesions—the arteritis of disseminated lupus, with its proliferation of the internal coat, thrombotic lesions, and fibrinoid degeneration of the smaller vessels. So I imagine that there will be numerous small infarcts found in different parts of the brain. Liver and spleen were enlarged. There was a gross albuminuria, and of course there was very limited renal function, as shown by a blood urea which I think at first was 60 and later rose to 80 and finally to 100 mg./100 ml. I should have made a comment about the initial symptoms that, while vomiting is a common symptom of uraemia, it is also a common symptom when associated with severe headache in malignant hypertension without uraemia at all. And I would have thought that, although a rise in blood urea is not in itself a serious thing but accompanies the accumulation of other poisons in the blood which cause symptoms, a blood urea of 60 to 80 mg./100 ml. was not sufficient to be accompanied by uraemic symptoms. One would not expect uraemic symptoms: the vomiting was due to malignant hypertension and not uraemia.

We come now to the reticulocytosis of 6.7%, and I would be interested to know what the haematologists think is the explanation of this. Haemolytic anaemia is well known to occur in disseminated lupus. But I don't see in the data we have been given any other evidence that there was an anaemia of the haemolytic type. I wonder whether this woman wasn't bleeding into the alimentary tract, as in fact we know she was bleeding into her skin, and whether her reticulocytosis was really due to haemorrhage—this is at any rate the suggestion which I put out. A white cell count of 9,000 is compatible with almost anything. In disseminated lupus perhaps most typically we have a leucopenia, but by no means always. There is a slight change in the serum proteins, about which I don't think I need comment. But I would very much like in the discussion to hear more about the anti-prothrombin type of circulating anticoagulant which was found. It has been found in other cases of disseminated lupus, and you will find mention of it in the classical article on disseminated

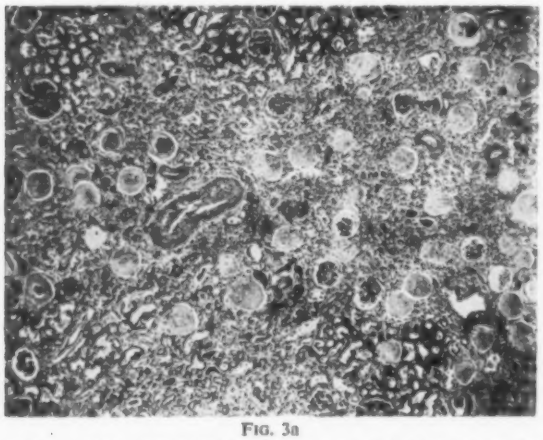

FIG. 3a

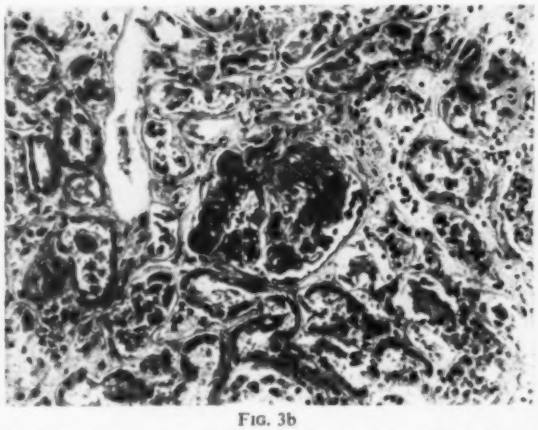

FIG. 3b

FIG. 3.—(*a*) Kidney (×34) showing a recanalized artery to the left of the picture and a wedge of ischaemic change to the right. (*b*) Glomerulus (×140) showing two hyaline thrombi.

lupus by McGehee Harvey *et al.** They found in some cases a substance of this kind which prevented or delayed coagulation in normal blood, so that it is evidently a circulating substance which causes this effect. They said that it was not a heparin-like substance, because its effect could not be reversed by protamine, which, as you know, reverses the heparin effect. That is all I know about it, and I would be very interested to know if the haematologists here were working on this interesting finding and if they found anything more.

A renal biopsy was done, but was not diagnostic. There was glomerular change, but then one would expect that for two reasons here—first of all there might have been the wire-loop lesion, so called, of disseminated lupus, and secondarily there may have been changes of malignant hypertension—fibrinoid necrosis of afferent arterioles and so forth—and the biopsy very well may not have been diagnostic. We missed, just reading quickly, the fact that L.E. cells (Fig. 2) were demonstrated. Well, that practically fixes the diagnosis, though different methods vary in the number of positives and negatives which are claimed in proved cases, and there are probably a few cases in which false positives occur. The radiological changes I don't think were particularly significant, the variation in the cardiac murmurs would be compatible with Libman–Sacks endocarditis, as would of course the improvement in these and other symptoms when the patient was given prednisone, but in spite of that a pericardial episode did develop, and this is very common in that disease. Hypertension was reasonably controlled so far as one can see, and as one would expect even without really first-class control the retinal lesions were reversible and the papilloedema resolved completely. We are not actually told whether the other signs of the retinopathy resolved, but I should fully expect that they did and that the treatment did not cause any rapid deterioration in the renal condition. The blood urea rose slowly as the months went on, as one would expect in this kind of disease. She was on mecamylamine, and, as you know from the paper by Harington and Kincaid-Smith,† if not from your own experience, this does in some cases produce that very distressing syndrome of mecamylamine tremor accompanied sometimes by a psychosis which is very alarming indeed, both to the patient, who is often aware of his mental state, and also to the nursing staff, who, in one of our cases, had cups and sputum pots and other things thrown violently at them. There was a letter in one of the journals which suggested that this was simply a manifestation of uraemia —well, I am quite sure we can rule that out. The *Folie Brightique* does not take that form. The muscular tremors are of different kind—they are muscular twitchings and jerkings, and so on—and I am sure that this is a syndrome which I have seen only in delirium tremens and mecamylamine poisoning. Our cases of mecamylamine poisoning have had a reduced renal excretory function, so that one assumes that high blood levels of the drug are kept up. One of them was a case which was very resistant to hypotensives and had to have large doses. Those are usually factors if the case goes wrong in this way.

This patient did develop pulmonary tuberculosis: the bacilli were actually found after many searches and she was given anti-tuberculous treatment. Tuberculosis was known as a complication of disseminated lupus even before these cases were treated by steroids. It may perhaps be more common now, but I don't suppose there is any statistical evidence on that subject. She was given chloroquine, which has been used in disseminated lupus —I don't know what the present views are on whether that is really of much benefit, except perhaps in the discoid type of lesion. We are not told whether she had a long illness accompanied by pyrexia, as so many of these patients do—or, shall we say, by episodes of pyrexia sometimes with long intervals in between—but we know disseminated lupus is a disease which occurs in very many different forms and no two case histories are alike.

Now, what I can't help you with, and I wish I could, is this extreme muscle weakness which seems to have been so definite a symptom in the last stages of the illness. One thinks immediately of potassium depletion. But we are told categorically by people who were looking out for this most carefully that the symptom could not be correlated with hypokalaemia, and was not improved by potassium supplements, and I should have thought that, although symptoms of hypokalaemia very often don't go absolutely *pari passu* with the height or rather the lowness of the serum potassium, nevertheless with adequate potassium supplements the response is usually very quick and one would expect it to be even quicker in a person whose excretory function was low; so I don't think the weakness can have been due to hypokalaemia. I did wonder, however, whether any studies of magnesium were done, but I only throw that out as a suggestion, because I know people are beginning to study magnesium in these kind of states. I think that is all I want to say.

Clinical Diagnosis

(1) Malignant hypertension secondary to focal ischaemic renal lesions resulting from the arteritis associated with acute disseminated lupus erythematosus.

(2) Libman–Sacks endocarditis.

(3) Bilateral cerebrovascular lesions due to lupus erythematosus.

(4) Pulmonary tuberculosis.

The Guest Speaker's diagnosis was the same.

Post-mortem Findings

Dr. B. E. HEARD: There was mooning of the face, the neck was thickened, the trunk was obese, but the limbs thin. There were numerous subcutaneous ecchymoses of the lower limbs. Both wrists showed ulnar deviation, and there was wasting of the muscles of the thenar and hypothenar eminences. Several fingers showed periungual fibrosis.

Both pleural sacs were obliterated by dense fibrous adhesions, particularly heavy on the right. The *right lung* showed a small focus of tuberculosis, 7 mm. in diameter, in the apical segment of the upper lobe. The rest of the lung was normal. The *left lung* was normal. Histologically the lesion was well localized and showed partly necrotic masses of macrophages surrounded by a thin mantle of lymphocytes and an outer zone of dense fibrosis.

The *heart* weighed 390 g. The mitral valve was slightly stenosed (70 mm.) and showed fibrosis of the cusps, slight shortening and thickening of the chordae tendineae, and pink vegetations up to 4 mm. across on the left halves of the auricular surface of the anterior and posterior cusps (Fig. 1). The vegetations extended

*Harvey, A. M., Shulman, L. E., Tumulty, P. A., Conley, L., and Schoenrich, E. H., *Medicine*, 1954, **33**, 291.

†Harington, M., and Kincaid-Smith, P., *Lancet*, 1958, **1**, 499.

down from the contact margins to the free margins. Histologically they were composed of masses of fused platelets separated by strands of fibrin. There was fibrinoid degeneration of the deeper part of the valve opposite one lesion and also of the superficial layers of the ventricular aspect. No inflammatory reaction was seen in the heart valves. The lesions were fairly characteristic of atypical verrucous endocarditis. There was no pericarditis, but the myocardium contained several small fibrous scars, and histologically there was no evidence of an active myocarditis. *Coronary arteries* and *aorta* showed mild atherosclerosis.

The *liver* (1,640 g.) was slightly enlarged and showed numerous minute yellowish-white nodules. Histologically these were small foci of necrosis.

The *kidneys* weighed 90 g. each, and were slightly shrunken. The capsules stripped with difficulty to reveal coarsely granular surfaces with nodules 3–4 mm. in diameter. The cut surface showed thinning and distortion of the cortex. Histologically there were wedges of ischaemic atrophy supplied by interlobular arteries showing evidence of previous thrombosis and recanalization (Fig. 3a). The glomeruli in these parts were shrunken and fibrosed but elsewhere showed changes frequently described in lupus nephritis. There were patches of thickening of the basement membrane of many glomerular tufts. There were foci of hypercellularity of lobulated glomerular tufts, occasional hyaline thrombi (Fig. 3b), and some capillary loops showing thickening and hyalinization. No typical "wire loops" were seen. The glomerular tufts were often adherent to the Bowman's capsules, and periglomerular fibrosis was frequently noted. There was secondary tubular atrophy with cast formation. Some interlobular arteries showed concentric fibrous thickening of the intima.

The *spleen* weighed 300 g. and was enlarged and firm. There was evidence of old perisplenitis and one old infarct was seen. Sections showed diminution in the quantity of white pulp (cortisone effect), and fibrous cuffs around central arteries, a common feature in disseminated lupus erythematosus.

The *thyroid* was normal, but the *adrenals* were reduced to approximately half of the normal size (7 g. combined) and histologically showed atrophy of the zona fasciculata and zona reticularis but persistence of the zona glomerulosa (cortisone effect). The *pituitary* showed some hyalinized basophils.

The *brain* weighed 1,295 g. (normal) and appeared slightly congested. 1-cm. frontal slices revealed several foci of cerebral softening in the frontal, parietal, and occipital cortex. Some of these may well have accounted for the symptoms a year before death. Sections showed intimal fibrous thickening, sometimes with recanalization of superficial cerebral arteries, but no evidence of an arteritis (media intact). The arteries of the circle of Willis appeared normal.

Pathologist's Diagnosis

(1) Disseminated lupus erythematosus.
(2) Libman–Sacks endocarditis.
(3) Lupus nephritis.
(4) Focal necrosis of liver.
(5) Cerebral softening (multiple foci).
(6) Pulmonary tuberculosis.

Discussion

Professor PLATT: Was there any evidence that she had a long feverish illness before you ever saw her, during the first nine years of her illness?

Dr. KINCAID-SMITH: There was no history of it.

Dr. C. PALLIS: There are two interesting neurological aspects of this case. The first is this bilateral pyramidal syndrome which seems to have occurred at the beginning of her illness. In view of the absence of any comment about a brisk jaw-jerk or of any spastic disorder of speech or swallowing one wonders whether the cause couldn't have been in the upper region of the cervical cord. I agree that cerebral infarction is more likely, but we are told that this patient had limitation of movement of her neck. We know that rheumatoid arthritis occasionally involves the atlanto-axial articulation, and it might be that she had some softening of the anterior ligament of the atlas and perhaps a slight degree of abnormal mobility between the odontoid and the anterior arch accounting for this spastic syndrome in the limbs, without any involvement of the cranial nerves. The other point concerns the terminal weakness, which was not associated with any sensory signs. I think myositis can occasionally occur in disseminated lupus; it certainly does in other collagen disorders like dermatomyositis. This might account for the absence of any biochemical abnormality.

Dr. C. M. FLETCHER: What about the muscle weakness? Are the pathologists unable to explain it?

Dr. HEARD: One section of voluntary muscle shows an area of necrosis, but there is no artery in it.

Dr. FLETCHER: Were the jerks preserved?

Dr. KINCAID-SMITH: Yes, they were increased throughout.

Dr. FLETCHER: There wasn't a generalized neuritis?

Dr. KINCAID-SMITH: No, not really.

Dr. I. MACINTYRE: Magnesium deficiency in rats is quite capable of causing both muscle necrosis and weakness.

Dr. PALLIS: Was the spinal cord examined at necropsy? Was a muscle biopsy performed in life?

Dr. HEARD: No.

Professor J. MCMICHAEL: The pyramidal tract lesions have been accounted for by the softening of the brain. When this patient came in with this double lesion—malignant hypertension probably related to polyarteritis and disseminated lupus—the therapeutic problem was indeed difficult. In spite of this she made a remarkable degree of temporary recovery for a few months before becoming seriously invalided again.

Dr. FLETCHER: Could I ask one other point about the natural history of this? She had been having phenylbutazone presumably from a doctor. Do you know whether she had ever had her blood pressure taken?

Dr. KINCAID-SMITH: It was taken the first time by a locum G.P. who saw her on the night of admission.

Professor PLATT: May I just make one comment on the phenylbutazone? When I came across that I naturally wondered whether some of the symptoms could be accounted for as a toxic reaction to it, but I came to the conclusion that they couldn't. It can of course cause

a thrombocytopenia and purpura, but usually I think in conjunction with a general aplastic anaemia.

Dr. J. G. SCADDING: There is one point about the streptomycin treatment. I take it the streptomycin was reduced in dosage because of the high blood urea?

Dr. KINCAID-SMITH: Yes. We did try to control the level with blood streptomycin estimations.

Dr. C. L. COPE: Isn't it worth making the point of how often we see disseminated lupus preceded by what was apparently quite typical rheumatoid arthritis, and before that by quite typical rheumatic fever? We have seen a number of examples of this in the last two or three years.

Dr. A. ST.J. DIXON: That is certainly so. The diagnosis of disseminated lupus suggests itself in any patient, particularly a young woman, who has rheumatoid arthritis and who develops signs of involvement of the viscera such as the development of a high blood pressure. This is the sort of case where one would have expected to get a positive differential agglutination test (Rose test). The experience with this test in disseminated lupus at the Manchester Royal Infirmary—if I may quote this in Professor Platt's presence—was that it was frequently positive, in over a third of all cases, I think, but when the question was looked into a little more closely it was found that nearly all the positives came from patients in the rheumatology wards, while nearly all the patients in the ordinary medical wards were negative.

Professor MCMICHAEL: Do you think we subdued the arthritis with cortisone?

Dr. HEARD: I suppose that's so. There was no activity in the knee-joint on histological examination.

Summing Up

Dr. KINCAID-SMITH: From the time that this patient was first admitted we believed that her kidneys would show an occlusive lesion of the interlobular renal arteries with associated focal areas of ischaemic atrophy such as have been demonstrated (see Fig. 3a), and that the hypertension was due to this lesion. Our reasons for thinking this were based chiefly on the rarity of malignant hypertension in association with the diffuse glomerular lesion of disseminated lupus and the fact that even where benign hypertension accompanies this glomerular involvement it is at a late stage of the illness when renal failure is well advanced. Occlusive vascular lesions have been described in vessels of interlobular size in disseminated lupus, and, as this is the vascular lesion which is commonly believed to cause severe hypertension in polyarteritis nodosa, we thought it was a far more likely cause of the hypertension in this case, in which the blood urea was only 60 mg./100 ml. This initial clinical hypothesis was substantiated by the renal biopsy, in which some glomeruli appeared quite normal, and by the fact that albuminuria virtually disappeared for a time during treatment. The latter occurrence would be very unlikely in the case of widespread glomerular lupus lesions. The glomerular lesions found at necropsy would appear, on clinical grounds, to have developed in the later months of the illness at the time of the increase in albuminuria and general deterioration.

We are grateful to Dr. J. P. Shillingford and Dr. B. Heard for assistance in preparing this report.

LEISHMANIASIS AMONG CHEWING-GUM COLLECTORS

Last month Professor P. C. C. GARNHAM and Dr. D. K. LEWIS reported to the Royal Society of Tropical Medicine and Hygiene on their investigations into the supposedly rising incidence of leishmaniasis in British Honduras, where the chewing-gum collectors are principally affected.

Chewing-gum apparently used to be made exclusively, and is still made partially, from latex gathered by bleeding the bark of the sapodilla trees which are numerous in the forests of British Honduras. The chicleros—as the latex collectors are called—live and work in groups of three or four. They enter the forests at the start of the rainy season, live a nomadic life moving from one camp to another, and only emerge after six months or more when the rains are over.

The chicleros were elusive subjects for study, but Professor Garnham and Dr. Lewis, proceeding through the forest on horseback, eventually discovered one of their camps near the forest-choked Maya ruins at Caracol. Further pursuit of small groups of chicleros fortunately proved to be unnecessary, for with the onset of the dry weather they began to leave the forests, convert their chicle into cash, and their cash into liquor in the bars of the townships and settlements. The best haul of active cases was obtained by visiting such an establishment at Benque, on the Guatemala border, where several were found, one midnight, listening and dancing to a marimba band.

Chicleros' Ulcer

Cutaneous leishmaniasis in this part of the world is largely confined to the ear and is known as chicleros' ulcer or "bay sore." The derivation of the latter is from the term "baymen" which has been used for the inhabitants living around the Bay of Honduras since the times of the original logwood-cutters there in the reign of Elizabeth I. An outstanding feature of the ulcers is their chronicity, some being of over 30 years' duration. In such cases there is destruction of the outer ear with granulomata alternately healing and ulcerating. Leishman–Donovan bodies are almost impossible to find except in relatively early lesions.

An animal reservoir for the causative parasite appears probable, for the chicleros are so sparsely distributed in the forest and stay for such a short time in one spot that the vector *Phlebotomus* would have little time or opportunity to acquire the infection from one person and pass it on to another a few weeks later. A search was therefore made for parasites in a variety of animals, including armadillos, the "protective armour" of which made cardiac puncture a difficult operation—compensated for, however, by the fact that the animals could later be killed and made very good eating. Fourteen species of *Phlebotomus* were found, including *P. cruciatus* Coquillett, which is believed to transmit cutaneous leishmaniasis in Mexico, but no leptomonads were found in the dissected flies. It was concluded that the most satisfactory control measure was likely to be the use of an attenuated vaccine.

In the discussion Dr. C. A. HOARE contrasted the multiplicity of clinical manifestations of leishmanial infection with the uniformity of the causative organism. He thought that, throughout the world, cutaneous leishmaniasis was caused by *Leishmania tropica*, but that the differing clinical states of "espundia," "uta," and chicleros' ulcer might be caused by subspecies. Professor A. W. WOODRUFF referred to the chronicity of chiclero ulcer and to the related problem of latency of both cutaneous and visceral leishmaniasis, describing cases in which the parasites had apparently lain dormant for years before declaring their presence in a clinically recognizable form. Professor H. S. SHORTT suggested that species of *Phlebotomus* flies dwelling only in the tree tops might account for the special vulnerability of chicleros to the local variety of cutaneous leishmaniasis; Dr. C. C. CHESTERMAN wondered if the curious localization of the chiclero ulcers at the tips of the ears might be the result of the parasite having an optimal temperature there for growth.

Drug Treatment of Disease

DRUG TREATMENT OF INFANTS AND CHILDREN SUFFERING FROM PNEUMONIA

BY

WILFRID GAISFORD, M.D., M.Sc., F.R.C.P.

Professor of Child Health and Paediatrics, University of Manchester

The treatment of infants with pneumonia has always differed from that of older children because of the different pathological conditions commonly encountered in the two groups—namely, bronchopneumonia in infants and lobar pneumonia in children. To-day, however, lobar pneumonia has become comparatively rare; this change is related to the higher incidence of viral infections and possibly to a decline in the prevalence of pneumococci. Viral infections of the lung tend to spread more widely and are seldom the cause of lobar consolidation. In infancy, when staphylococci, *Haemophilus influenzae*, or Friedländer's bacillus are more likely causative organisms than pneumococci, the lesion resulting is usually bronchopneumonia. The same, or similar, drugs are therefore indicated in most cases for both age groups.

It is easy to say that the drug which should be used is the one to which the infecting organism proves most sensitive, but it is singularly difficult to ascertain with any degree of certainty what the infecting organism is in young children, who notoriously swallow what sputum they produce, and it is unwise to withhold treatment pending the results of any investigations. This has naturally led to the prescription of one or more of the "broad-spectrum" antibiotics from the outset, and it is indeed difficult not to uphold this rationale on occasions. What *is* important is that chemotherapy should not be used merely as a febrifuge. Aspirin is just as effective in reducing fever and much less dangerous. Not every infant with a cough and fever is starting bronchopneumonia; definite physical signs should be evident before a course of antibiotic therapy is prescribed.

Lobar Pneumonia

As lobar pneumonia, though less frequently seen than formerly, still occurs and is the most straightforward pulmonary infection to be encountered, the appropriate drug therapy for affected children will be described first. "Stosstherapy," the large single dose, is the treatment *par excellence* and is nearly always successful. Sulphonamides are the first choice. Sulphapyridine is the most active against pneumococci, but, because it is more toxic than the later compounds, it is little used now. Of the later compounds, sulphadiazine, sulphathiazole, and sulphadimidine are all reliable and efficient. It is wise to combine two or more sulphonamides, because this diminishes the risk of renal complications; sulphamerazine in particular has been reported as causing crystalluria and is therefore better avoided, especially in young children, whose urinary output may be difficult to assess with any certainty. The diazine, thiazole, and dimidine compounds may well be prescribed in equal parts. At 2 years of age 1 g. of this mixture would be an adequate dose; at 3 years, 1.5 g.; and from 4–5 years, 2 g. It is seldom necessary to exceed 3 g. in childhood. Sulphafurazole is also of value and has the advantage of more ready solubility; the dose is the same as for the triple mixture.

If vomiting is a prominent feature, or if the drug is vomited when administered, penicillin should be given intramuscularly. From 1,000,000 units at 2 years to 2,000,000 units at 5 years of age should be sufficient. In either case no further specific treatment should be necessary for acute pneumococcal lobar pneumonia.

Attention thereafter is directed solely to the child's general condition and not to the physicial signs in the lungs: these will follow the normal course, and their disappearance is in no way expedited by the stoss-therapy. In other words, the continued presence of slight fever and the persistence of bronchial breathing for two to three days are not an indication for further treatment, provided the child's general condition is steadily improving.

If, in the early stages, a frequent, irritable and painful cough is present, Gee's linctus (linctus scillae opiatus *B.N.F.*) may be given in doses of 30–60 minims (1.7–3.5 ml.) until relief is obtained. No other drug therapy is required.

Bronchopneumonia

In the treatment of infants with bronchopneumonia it is always helpful if there are any indications of the nature of the causative organism. In the presence of epidemics, or of the infection previously of an older sibling or adult in the household, it is possible that the organism may be known and the most suitable antibiotic be thereby determined. Similarly, in the newborn period it is likely that the organism will be a staphylococcus or *Escherichia coli*. Pertussis, even in unimmunized infants, may not be accompanied by whooping, and the diagnosis will be suspected from the spasmodic nature of the cough, by its being worse at night, and by many of the spasms ending in a bout of vomiting.

Unfortunately bronchopneumonic infants are not good subjects for stosstherapy; nevertheless, every attempt should be made to give maximal dosage of whatever antibiotic is chosen and to give this for the shortest possible time. No antibiotic acts selectively on the lungs and all are apt to exert unfavourable influences elsewhere in the body. In infants one special risk is that of thrush, which in the presence of antibiotics appears to have an enhanced virulence. Moreover, it may not only spread from the mouth to the gut but even enter the smaller blood vessels and become systemically disseminated, with grave risk of fatal pulmonary moniliasis. Further, it is well known that antibiotics administered for any length of time interfere with the natural intestinal synthesis of members of the vitamin-B complex, and they may induce diarrhoea, which will add greatly to an infant's task in successfully overcoming his bronchopneumonia. If, for any reason, treatment has to be

continued for more than a week, extra vitamin B should be given throughout the subsequent course.

Whether an antimonilial drug should also be given prophylactically is more debatable. It is probably preferable to exercise greater care with the oral hygiene and with the preparation of the infant's feeds, because the prophylactic use of such drugs as nystatin may indeed lead to the emergence of resistant monilia organisms if they succeed in gaining entry into the infant's mouth in his debilitated condition.

Neonatal Pneumonia

Newborn infants may acquire a pneumonic infection before, during, or immediately after birth. In the first two cases some knowledge of the infecting organism may be gained from bacteriological examination of the mother (blood culture, culture of the liquor amnii, or culture from a high vaginal swab). In the case of infection acquired in the newborn period the organism will usually be a staphylococcus or *E. coli*.

The chief difference in treatment depends on whether the infant has been born in hospital or at home, because the chances of a penicillin-resistant staphylococcus in hospital are too great to allow of the use of penicillin as the antibiotic of choice. At home, penicillin will probably be successful. In hospital, streptomycin is the most useful drug and may be prescribed in doses of 125 mg. twice a day intramuscularly (62.5 mg. for infants weighing less than 5 lb. (2.25 kg.)), usually for two or three days. At home crystalline penicillin, 250,000 units, should be injected as soon as the diagnosis is suspected, followed by procaine penicillin 250,000 units daily until the infection is controlled. If there is reason to believe that *E. coli* is the infective organism, streptomycin should be given as above. If there has been no response to penicillin, prompt change to streptomycin should be made because lack of response would suggest that the organism was either resistant or insensitive to penicillin. In older infants the choice of the main drug will be determined, as previously indicated, if there is any clue to the likely organism—for example, chloramphenicol in pertussis—the dose varying from 125 to 250 mg. every 4–6 hours. Treatment should preferably be discontinued after a week or ten days. The risks of producing aplastic anaemia are remote when compared with the good results which may be expected from this antibiotic. Chloramphenicol is likewise indicated if *H. influenzae* is suspected, but treatment does not usually need to be continued for so long.

Pneumonitis

In the recurring episodes of pneumonitis to which infants with mucoviscidosis (cystic fibrosis of the pancreas) are so often subject, chlortetracycline ("aureomycin") is the antibiotic of choice. Its dose is the same as that of chloramphenicol. It may indeed also be used, in smaller dosage, as a continuous prophylactic, but, if it is, regular bacteriological examination of the flora should be undertaken. In these cases the main infecting organism is the staphylococcus, but after continued treatment with chlortetracycline *E. coli* may become dominant, and then the antibiotic should be changed.

When infants have repeated attacks of lower respiratory infection, a search for the underlying pathological condition must not be omitted. There may be a congenital cystic lung, for example, or the infections may be due to a general disorder such as agammaglobulinaemia. Investigation should therefore include examination of the sweat, bronchography, and plasma electrophoresis—each providing positive evidence of mucoviscidosis, cystic lung, and agammaglobulinaemia respectively.

Of the many other antibiotics available, all may be of value if resistant strains of organisms are present and should be tried if adequate response is not forthcoming after the treatment already recommended for the conditions described. There is seldom any indication for combined antibiotic therapy. Synergism is rare, and there is no great advantage in combinations which are simply additive. *Moreover, if the dose prescribed of any of the various members of a mixture is suboptimal, antagonism may occur and resistant organisms may emerge.*

Virus Infections

There remain the infections caused by viruses—an important and seemingly growing group—for which there is no specific treatment yet. Antibiotics may give rise to resistant organisms; erythromycin and novobiocin are perhaps least likely to do so, but they should be kept for special cases and not used in the first instance except in an epidemic in which other antibiotics have proved valueless and one or other of these has proved helpful. The dose is 50–100 mg. 8-hourly. A recent introduction is an intramuscular preparation of erythromycin (50 mg. of erythromycin ethylsuccinate in 1 ml. propylene glycol), which may prove of special value in acutely ill infants and children and when vomiting is a feature of the illness. Parenteral treatment should be replaced by oral therapy as soon as possible.

In the initial treatment of an infant with bronchopneumonia it is usually as well to assume a bacterial origin and to prescribe a broad-spectrum antibiotic of the tetracycline group (aureomycin, "terramycin," "achromycin"). The dose should be about 25–50 mg. per lb. body weight per day (12–25 mg. per kg.). Failure of response within two to three days would suggest that the infection was viral; the only value then of continuing antibiotics would be to prevent secondary infection, but it is probably preferable to revert to penicillin if such cover is thought necessary. A suspension of potassium phenoxymethylpenicillin (penicillin V) given by mouth may well be as beneficial as intramuscular injection and certainly makes management of the infant easier. The dose is 30–60 minims (1.7–3.5 ml.) twice a day. This is the equivalent of 100,000 to 200,000 units of crystalline penicillin twice daily. Treatment should always be continued until the infant's general condition is satisfactory and the temperature has been normal for 24 hours.

Symptomatic Treatment

Symptomatic treatment may be of value in addition to chemotherapy. Cough is often troublesome in infants with bronchopneumonia, and on auscultation there are usually copious moist rales. A mixture such as the following may then be prescribed, a teaspoonful diluted to be taken three or four times a day.

Ammonium carbonate ...	2½ gr. (160 mg.)
Sodium bicarbonate	2½ gr. (160 mg.)
Potassium iodide	1 gr. (65 mg.)
Liquid extract of liquorice ...	10 minims (0.6 ml.)
Peppermint water to 60 minims (3.5 ml.)	

If spasm is a feature, relief may follow the administration of an antihistaminic combined with a sedative. Suitable drugs are mepyramine maleate

(*Continued at foot of next page*)

To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Strepsils Antiseptic Lozenges (Boots).—Each lozenge contains 2:4-dichlorobenzyl alcohol 1.2 mg. and amyl-*m*-cresol (6-pentyl-*m*-cresol) 0.6 mg. in a hard sugar base. This also is an antibacterial preparation for local use against minor infections of the mouth and pharynx.

Iversal (Farbenfabriken Bayer (Distributors : Levmedic)).—Each troche contains ambazone (1 : 4-benzoquinone aminohydrazine thiosemicarbazone hydrate), 10 mg. This inhibits the growth of haemolytic streptococci and pneumococci in high dilution but has no action against coliform bacteria, and so will probably not disturb the intestinal flora.

Neither of these preparations contains any of the more generally used antibacterial agents, and organisms resistant to them are unlikely to cause trouble. They may therefore have some value in treating minor infections in the mouth and pharynx, but are not likely to be suitable if a severe buccal or pharyngeal infection develops, when antibacterial drugs given systemically would be indicated.

N.H.S. basic price : strepsils, 24 lozenges, 1s. 8d. ; iversal, 15 troches, 2s. 4d.

Steroxin Ointment and Dusting Powder (Geigy).—These are chloroquinaldol 3% in an ointment (non-greasy base) and 5% in a dusting powder.

Although superficial infections of the skin are very often treated with antibiotic ointments, an antiseptic such as steroxin still has a valuable place. It is perhaps most useful in superficial infections such as intertrigo, moist infected seborrhoeic dermatitis, infectious eczematoid dermatitis, and other types of eczema with superadded secondary infection. The response of lesions of this kind to treatment is often difficult to predict, and it is easy to make the eruption worse with an application which is irritant or sensitizing. In the treatment of these difficult eruptions steroxin occupies an honourable position ; in effectiveness it compares well with many of its rivals and it is very unlikely to irritate. It can be combined with other bases such as Lassar's paste and it can be mixed with hydrocortisone ointment, sometimes with great benefit.

N.H.S. basic price : 4 oz. ointment, 6s. ; 30 g. powder, 1s. 8d.

(Continued from previous page)

(" anthisan ") 5–25 mg. with pethidine 5–10 mg., the lower dose being suitable for infants of under 6 months and the higher for those between 6 months and 1 year of age. This may be repeated as necessary.

Finally, although tuberculosis is much less common in infants and children than it was, it still occurs. The value of the Mantoux test must not be overlooked, for in tuberculous bronchopneumonia the substitution of isoniazid and streptomycin for other antibiotics tried previously will rapidly improve the child's condition. But the treatment of tuberculosis will not be discussed in detail here.

In overwhelming infections, both tuberculous and non-tuberculous, steroid therapy may prove life-saving. Hydrocortisone, given by mouth in doses of 5–10 mg. twice daily for three or four days, should certainly be tried, provided always that it is accompanied by adequate antibiotic therapy.

Correspondence

Aetiology of Coronary Disease

SIR,—Dr. J. N. Morris and Dr. Margaret D. Crawford (*Journal*, December 20, p. 1485) have given us a fascinating study of the relationship between coronary heart disease and physical activity of work. I hope they will extend their inquiries, for, although other studies in which they are engaged on somatotype and occupation may add something, they have, as they themselves remark, shed no light so far on the personality factors involved both in taking exercise or, for that matter, in taking this or that form of diet.

Recently at the request of Dr. S. Savage, who for preventive purposes was seeking some quick and suitable means of recognizing people predisposed to coronary disease, I calculated the frequency per thousand of various somatotypes in the series of young men with coronary thrombosis reported by Gertler and White.[1] Next I calculated the frequency per thousand of similar somatotype groups in W. H. Sheldon's distribution of 46,000 American men. Dividing the first frequency by the second gives a ratio which indicates which somatotypes succumb most often to coronary thrombosis in early middle life, and which types are relatively free. An abbreviated list of results is given below in which the ratios have been multiplied by 100 to express the risk of coronary disease as a percentage of general expectation. Descriptions of physique in each somatotype sector may be found elsewhere.[2]

		Percentage of General Expectation
Somatotypes Highly Disposed		
Sector Mf	Near somatotype 451	1,915
	Near somatotypes 352, 353	440
	Near somatotypes 461, 361, 362	314
Sector Fm	Near somatotypes 641, 541	757
Somatotypes Less Disposed		
Sector Ml	Central	21
Lm	Central	51
Lf	Central	55
Lm	Peripheral	rare
Lf	Peripheral	rare
Fl	Central and peripheral	rare

Thus, although it is a dominantly muscular build which seems most disposed, it is the fat muscular build which carries much the highest risk. The risk for lean muscular builds is lower and they may include more bus conductors than drivers in their ranks, more postmen than Government clerks. Physical disposition to coronary disease appears to vary from negligible levels of risk to levels 10 or perhaps 20 times general expectation. That this risk may be recognized in terms of physique makes it possible for men most in need to take precautions, while those of more linear build, who incidentally are more often prone to anxiety, may be exempted from unwelcome exercise, spared unnecessary restriction or alteration in their diet, and relieved of inappropriate foreboding.—I am, etc.,

R. W. PARNELL.

The Warneford Hospital, Oxford.

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1 Gertler, M. M., and White, P. D., *Coronary Heart Disease in Young Adults*, 1954. Harvard University Press, Cambridge, Mass.

2 Parnell, R. W., *Behaviour and Physique*, 1958. Edward Arnold, London.

Hospital Sterilization

SIR,—Your leading article (*Journal*, December 27, p. 1582) on the report of the Nuffield Provincial Hospitals Trust[1] suggests that cardboard dressings boxes might be out of place in an operating theatre because "material like cardboard is loaded with spores." In this hospital bacteriological examination of homogenized samples of cardboard from such boxes has confirmed the presence of *Clostridia*; organisms so far identified morphologically and biochemically include *Cl. tetani*, *Cl. welchii*, and *Cl. sporogenes*.

Exposure of the cardboard to phase-boundary steam at 121° C. (250° F.) for two minutes before homogenization was sufficient to kill the organisms present, and examination of 30 samples of cardboard has shown no *Clostridia* with a greater moist-heat resistance. These findings agree with the figures for the moist-heat resistance of *Clostridia* reviewed by Kelsey.[2] Perkins[3] states that "none of the pathogenic organisms have [*sic*] been shown to be resistant to an exposure of even three minutes" at 121° C. (250° F.). Such moist-heat resistance is easily dealt with by efficient steam-sterilizing equipment of the gravity air-displacement or high-pressure high-vacuum type, and the manufacturers have agreed to sterilize the boxes before sale.[1] The use of cardboard dressings boxes should not, therefore, add to the risks of infection already faced by the hospital patient.—I am, etc.,

Queen Alexandra Military Hospital, London, S.W.1. A. C. SCOTT.

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[1] *Present Sterilizing Practice in Six Hospitals*, 1958. Nuffield Provincials Hospitals Trust, London.
[2] Kelsey, J. C., *Lancet*, 1958, 1, 306.
[3] Perkins, J. J., *Principles and Methods of Sterilization*, 1956, p. 41. Springfield, Illinois.

Sulphonamide Mixtures

SIR,—Your annotation (*Journal*, January 3, p. 40) states that, "Though the evidence suggests that sulphonamide mixtures had advantages over the less soluble sulphonamides when used alone, it seems rather doubtful if this holds for the more recently introduced drugs in this group." I, also, doubt whether a mixture of sulphonamides has any advantage over a single sulphonamide of the type you mention, and this has been borne out by my experience with the use of sulphafurazole ("gantrisin") in the treatment of urinary infections in infancy and childhood.

During the past three years, 44 children varying in age from 1 month to 14 years having a proved urinary infection, with leucocytes and casts on microscopic examination of the urine and a growth of *E. coli* or *B. proteus* on culture, have been treated. Of these, 34 children received sulphafurazole in the form of a pleasant-tasting suspension, 0.5 g. being given four-hourly in the under-5 age-group and twice this amount in the older children, for a period of three to five days; at the end of this time, only six still showed residual infection in the urine requiring further treatment. In no case was any toxic reaction recorded.

Sulphafurazole therapy was started in these children while waiting for the laboratory report on the sensitivity of the organism, and the clinical results justified the drug having been used as first choice, even though, in several cases, the laboratory report suggested *in vitro* resistance to sulphonamides.

In these days, when general practitioners and hospital staff are constantly being reminded of the increasing cost of the drug bill in the National Health Service, due at least partly to the wide use of antibiotics, it is useful to remember that in sulphafurazole there is available a safe, reliable, and pleasant sulphonamide for the treatment of urinary infections so common in children.—I am, etc.,

Department of Paediatrics, Bury and Rochdale Hospitals. B. WOLMAN.

Acute Pancreatitis

SIR,—We are interested in the observations by Mr. A. V. Pollack (*Journal*, January 3, p. 6) on the use of corticotrophin in acute pancreatitis and his failure to obtain any significant results. We[1] used cortisone and/or prednisone, since we considered that one of the factors concerned in the high mortality of acute haemorrhagic pancreatitis might well be adrenal failure. Should this indeed be so, then results of treatment with corticotrophin are not likely to be good.

The experimental production of pancreatitis by cortisone administration may not be relevant to the problem, since in acute pancreatitis corticoids are administered for a relatively short time to patients with an already seriously disorganized pancreas.—We are, etc.,

The General Hospital, Birmingham, 4. M. J. MEYNELL. W. T. COOKE.

REFERENCE

[1] Rogers, N. C., Wilson, A. O., Meynell, M. J., and Cooke, W. T., *Lancet*, 1956, 2, 651.

Thyroid Neoplasms and Irradiation

SIR,—I have read with great interest the papers by Professor G. M. Wilson and his colleagues and by Dr. A. W. G. Goolden on thyroid neoplasms following irradiation (*Journal*, October 18, pp. 929 and 954), and would like to congratulate the authors for reporting these cases. I believe that it is the duty of each department specializing in thyroid diseases to collect such cases and to try in extensive series to evaluate quantitatively the carcinogenic risk associated with irradiation of the thyroid gland during childhood.

In our series of thyroid cancer[1 2] we have found six patients with cancer of the thyroid who had had irradiation of the neck prior to the onset of the disease: three among 11 children under 14 years of age, and three among 160 adults. Below are the details of the three adults.

Case 1.—Female irradiated for a tachycardy at the age of 15. Although no goitre was noted, a hyperthyroid syndrome was suspected and radiotherapy of the thyroid region was performed. It was impossible to obtain detailed information about this treatment, since it was given in 1908. It was sufficiently intense, however, to induce a severe cutaneous reaction—permanent sclerous atrophy of the dermis and epidermis, and telangiectases. 44 years later, in 1952, a cancer of the thyroid gland appeared (Hürthle-cell cancer).

Case 2.—Female treated for a laryngeal papillomatosis at the age of 7. 29 years later, at 36 years of age, a cancer of the thyroid gland appeared (vesiculo-trabecular).

Case 3.—Female treated intensively by *x* rays at the age of 5 for a laryngeal papillomatosis. This treatment was so intense that a tracheotomy was necessary a few years later. At the age of 26, 19 years later, a vesiculo-trabecular type of cancer of the thyroid gland appeared.

The most interesting feature of all the cases published so far seems to be that most of them were irradiated before the age of 20 years. Obviously large-scale

surveys are needed to evaluate how much irradiation of the neck during childhood increases the incidence of thyroid cancer in adult life.—I am, etc.,

M. TUBIANA.

Service des Isotopes et des Radiations de Haute Energie, Institut Gustave-Roussy, Villejuif, France.

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[1] Coliez, R., Tubiana, M., Dutreix, J. M., and Laugier, A., *Bull. Ass. franç. Cancer*, 1956, **43**, 218.

[2] Tubiana, M., in *Proceedings of Conference on Radioiodine*, 1956, 185–190, Acrh–100. University of Chicago Publ.

Hypothermic Myxoedema Coma

SIR,—In the *Journal* of November 8 (p. 1144), we have read with great interest an article by Dr. Donald W. Macdonald about hypothermic myxoedema coma. As we have treated two very similar cases we would like to notify an important observation made by Dr. Macdonald but insufficiently stressed; nor is it emphasized in other reports of myxoedema coma.

Our cases were two women 68 and 77 years of age who both showed on arrival at hospital all the typical clinical signs of severe myxoedema. The laboratory findings confirmed the diagnosis. When these patients became unconscious because of their myxoedema, their respiration almost ceased. The acid-base balance of the blood showed then a marked respiratory acidosis. The values were, in our first case, serum pCO_2 109 mm. Hg and *p*H (38° C.) 7.22; in the second case, serum pCO_2 86 mm. Hg. and *p*H (38° C.) 7.08. The difference in *p*H between the two cases was due to compensatory metabolic alkalosis in the first case. The standardized bicarbonate value was 38 mEq/l. (corrected to pCO_2 40 mm. Hg and oxygen saturation of 100%). The corresponding value for our second case was normal (19 mEq/l.).

The first step of treatment was tracheal intubation and artificial ventilation with mask and bag. Both patients regained consciousness within ten minutes. However, their respiration was still insufficient and it became necessary to treat them in a respirator for two weeks. We had to do so in order to keep their carbon-dioxide tension within normal limits and to prevent them becoming comatose again. During the time in the respirator the patients were given triiodothyronine and L-thyroxine respectively. Their hypothermia ceased within one day without further treatment. After the improvement of their hypothyroid status the patients could manage their respiration without carbon-dioxide retention. They lived, respectively, for one and a half years and three months after the acute episode, and died of intercurrent diseases.

In cases of severe myxoedema we find it of the greatest importance to prevent and treat carbon-dioxide retention.—We are, etc.,

P. NORDQVIST. K. STENBERG.
K. G. DHUNÉR. G. ÖRNDAHL.

Departments of Medicine and Anaesthesia, Sahlgren's Hospital, University of Gothenburg, Sweden.

Cullen's Sign

SIR,—After reading Dr. E. F. B. Cadman's article on Cullen's sign (*Journal*, September 20, p. 718), I should like to mention a case that we have had occasion to study recently at the Internal Department of the Hospital in Jihlava.

S. J., 63 years, treated before in our department for bronchial asthma, pulmonary emphysema, and chronic cor pulmonale. He was accepted again on June 20, 1958. Beside the conditions mentioned above, he had severe pain in the epigastrium and had vomited. The pain was limited to the epigastrium, and the patient was agitated. On examination we found the liver to be enlarged three fingers below the costal margin and tender on palpation. As the dyspnoea got worse we considered acute right ventricular failure with hepatomegaly, and later also an acute abdomen. The patient was seen by a surgeon, but was not operated upon because of his critical state. The pain gradually became milder, the epigastrium, while remaining tender, was not so rigid, but the enlargement of the liver diminished little. After three weeks we observed a blue, hourglass-shaped discoloration above and below the umbilicus. The width of its base was 15 cm., the length 20 cm. Because of this sign we thought of pancreatitis. At the same time auricular fibrillation occurred, and the cardiac insufficiency became rather worse; digitalis and diuretics were administered instead of strophanthin. The sign of the clear-cut supra- and infra-umbilical, hourglass-shaped area remained for three days, then its base became narrower and the margins indistinct, until after 10 days there was hardly any trace of it left.

The patient died after six weeks, with progressive heart failure and severe dyspnoea. In the last weeks the dyspnoea was due rather to his emphysema, and the typical asthmatic attacks were absent. At necropsy massive emboli were found in the branches of the pulmonary artery, with pulmonary infarction and hepatomegaly (chronic venostasis with incipient cardiac cirrhosis). Thus the clinical diagnosis was confirmed. The pancreas macroscopically and histologically was normal.

In our opinion the blue, hourglass-shaped discoloration was associated with the acute enlargement of the liver as a symptom of the right ventricular failure precipitated by the emboli in the branches of the pulmonary artery.—I am, etc.,

J. VACHTENHEIM.

Jihlaya, Czechoslovakia.

Carbon-monoxide Poisoning

SIR,—Your issue of December 27 has just reached me here, and I hope it is not too late to add a word to the correspondence on carbon-monoxide poisoning which Dr. H. L. Marriott initiated in that issue (p. 1591). You will recall that you published recently a contribution toward the study of carbon-monoxide poisoning by Apthorp *et al.*,[1] in which some experimental evidence was given of the relative efficacy of oxygen and carbon dioxide in resuscitation from carbon-monoxide poisoning. As stated in the introduction to that paper, the experiments were designed to provide data to enable the relative merits of different procedures for resuscitation to be assessed. We concluded that the administration of carbon dioxide is only indicated if it could be observed to be producing hyperventilation in the patient being treated.

It is quite clear that the prolonged discussion which has been carried on between Dr. Marriott and the Medical Research Council will only be satisfactorily settled when there is information on the level of arterial carbon-dioxide tension found in patients who have been poisoned with carbon monoxide. The question as to whether or not carbon dioxide should be used in any form in resuscitation hinges entirely on whether or not in the majority of cases of carbon-monoxide poisoning there is or is not significant carbon-dioxide retention at the time the patients are first seen. This information would be very easy to obtain and is urgently needed. One might draw attention to the fact that within the last two years physiologists have provided very significant evidence that acute carbon-dioxide retention with an increase of carbon-dioxide tension in the blood to values as relatively low as 70 mm. Hg will exert considerable depressant effect on the myocardium. This important

new evidence suggests that the final result of severe carbon - monoxide intoxication with respiratory depression may be the result of circulatory depression imposed on tissue anoxia. This possibility suggests that carbon-dioxide administration should be very cautiously undertaken if it is shown that in the majority of cases of carbon-monoxide poisoning there is significant carbon-dioxide retention at the time the patient is first seen.—I am, etc.,

D. V. BATES.

Department of Medicine,
Royal Victoria Hospital, Montreal.

REFERENCE

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Safety Cap for Motorists

SIR,—The most common area injured in survivors of motor-cycle and car crashes is the skull and its contents, either as isolated lesions or more frequently associated with injuries to other parts of the body. Protection of the skull is of extreme importance, not only to save its contents from the more severe forms of injury, but to maintain the conscious state of the injured so that they are capable of giving clear expression to their symptoms and display signs that will permit an early diagnosis of other injuries on which their life may well depend. Patients deeply unconscious from head injury can pose the most difficult problems in diagnosis of associated severe lesions, particularly of the abdominal contents.

Against this factual background of the frequency of head injury and the difficulties of diagnosis in an unconscious patient, I am surprised that less than 50% of motor-cyclists now wear crash helmets. For many years I have collected crash helmets from injured motor-cyclists admitted to the hospital I serve. Often the helmet has been smashed beyond repair but the patient has not suffered even a scalp abrasion. More important, they have been conscious and have expressed their symptoms and displayed signs that have led to the vital early diagnosis of associated injuries. More surprisingly car occupants wear no head protection at all, yet approximately 60% of their injuries involve the head. Almost all men and many women, when getting into a car, immediately discard their hats or caps, yet most British headwear is made of felt, one of the best materials to absorb and spread the violence of any direct impact on the skull; even the wearing of a normal hat has at least some protection.

Recently I visited the British Hat and Allied Felt Makers Research Association at Droylsden. There I was shown a normal-looking, comfortable, and light cap, with the crown reinforced with No. 11 felt and the peak with felt and foamed plastic. On bench test this cap absorbed approximately 60% of the violence of a 4,000 lb. (1,816 kg.) impact—5,000 lb. (2,270 kg.) is estimated as the force necessary to fracture a skull and very little more is required to disintegrate the brain. I was so impressed with the protective value of this completely normal-looking cap that it has since become an essential part of my car's equipment. If every car occupant wore such protection and every driver resolved to keep his maximum speed down to 60 miles/hour (96 km./hour), then this country's hospitals would be relieved of a large number of insoluble curative problems and, equally important, we would see fewer unconscious patients and thus be able to make the essential *early* diagnosis of associated severe injuries. Many accident victims, too, would be relieved of troublesome headaches and the more severe aftermaths of major cerebral injury.—I am, etc.,

Birmingham Accident Hospital. WILLIAM GISSANE.

Three Pillars of Clinical Research

SIR,—Mr. Ian W. Payne (*Journal*, January 17, p. 173) flatters me by the imputation that I pressed home my point that surgeons were, on the whole, bad at mathematics by producing an example in my own paper. This is a perfectly splendid idea and I wish I had thought of it, but unfortunately it is just not true. Mr. Payne says, "Surely a high maximum should automatically increase the range of marking." It should indeed, but often it does not. He goes on to describe a system of marking by percentages which are then adjusted in the ratio of the permitted maxima. Nothing could be more satisfactory—in fact it is what, in other words, I recommended; but again this does not happen to be done in the majority of examinations. If it were done, I should not have mentioned the matter.

"To take an exaggerated example," he says, "if the papers were marked out of 10, and the clinical out of 490 marks, it would scarcely be worth the effort of writing the paper." By his excellent system this is true. In the system prevailing in most of the surgical examinations in which I have acted as an examiner what would happen is that A would get 6 marks in the paper to B's 5; while A would get 249 in the clinical to B's 250, making a total of 255 each—that is, if my arithmetic is correct, and, as Mr. Payne says, one can always get this checked by an expert.—I am, etc.,

London, N.W.1. H. J. B. ATKINS.

"Your Figures in their Hands"

SIR,—Your leading article (*Journal*, January 10, p. 101) criticized the methods employed by the B.B.C. in attempting to assess some of the effects of the television series "Your Life in their Hands." May I concentrate my reply on three of your points?

(1) You say that "it is by no means clear that this technique (of inviting viewers to attend meetings) was ever likely to lead to a sample representative of TV owners." Most statisticians would certainly prefer to work with carefully chosen random samples of the population, but it should be remembered that almost certainly the majority of the sample inquiries carried out nowadays do *not* use such methods. To do so is often either impracticable or too expensive, or both. The practice of studying the effects of a series of broadcasts by inviting samples of viewers to attend group meetings is not new. We employ this method quite frequently and are satisfied, from our experience, that it yields samples not seriously unrepresentative of the adult viewing public. For an explanation of the apparently low response rate (30% to 40% of those invited) we need not look any further than the fact that those invited were given a very limited choice of evening on which to attend, and, as our report says, on this occasion the situation was made more difficult by reason of the bus strike. Had the invitation made any reference to the series which was to be the subject of the inquiry, then indeed it would not be unlikely that acceptance, or failure to accept, would have been associated with reaction to the series. In fact, as the report made clear, the invitation contained no such reference; indeed, the purpose of the inquiry was not disclosed until the process of questioning in the meetings was nearly complete.

(2) "Having got our sample of viewers," we then assessed the effects of the series by using a method of matching. This, also, is by no means new or

invalidated. You suggest that the best way to measure effects is to study the same individuals before and after they view the series, but this would only be so if the pre-broadcast study did not itself affect the sample. We prefer the process of matching, which, far from being as you describe "an astonishingly crude method," is, in fact, a delicate and sensitive operation. While it cannot always guarantee success, it is much more likely to isolate the real effects of the series than is the "before and after" technique.

(3) From your final paragraph it would seem that you are under some misapprehension about the object of the inquiry. It did not, and indeed could not, study the effects of the series on small subgroups of the population, such as "the unstable with a morbid curiosity about blood and bowels." In the absence of inquiry, "how the series affected" this group is, I suggest, still an open question.—I am, etc.,

R. J. E. SILVEY,
Head of Audience Research,
British Broadcasting Corporation.

London, W.1.

*** The inquiry's object, as stated in the B.B.C.'s Audience Research report, was to investigate: "The extent to which the series (i) affected viewers' worries with particular reference to illness in general, (ii) affected anxiety, (iii) stimulated hypochondria, (iv) affected worries about specific illnesses . . . (etc.)." Mr. Silvey now says the inquiry did not, "and indeed could not," study the effects of the series on small sub-groups of the population. But it is with just such specially vulnerable "small sub-groups" that doctors are concerned.—ED., *B.M.J.*

Recurrent Cancer

SIR,—I would like to congratulate Mr. K. Cronin and Mr. H. Ellis on their article (*Journal*, November 29, p. 1319) and the "message" which they have passed on—viz., recurrence of cancer in the alimentary tract is by no means a hopeless state of affairs. Recurrent cancer in other parts of the body is just as amenable to further treatment as is recurrent cancer in the alimentary tract. Brunschwig has amply illustrated this at Memorial Center in New York; cancer of the cervix which recurs after radiotherapy is usually resectable by means of pelvic exenteration (anterior or posterior or total), and I have been privileged to see some of his early cases which have now survived 10 years. Recurrent skin cancers, recurrence of cancer of the mouth, local recurrence of melanoma, recurrent neuroblastoma, to quote but a few examples, are often amenable to further surgery.

Similarly, just as recurrent cancer is often worthy of reoperation, so is cancer which has been treated inadequately. I can recall a patient in New York who twice appeared to have had this misfortune. He had had a partial gastrectomy for cancer in another country, but it was soon apparent that this operation had been inadequate. A total gastrectomy was performed in New York and the patient returned home and remained well for over five years; he then developed pain in the right iliac fossa and underwent appendicectomy, apparently for acute appendicitis. But all was not well, because he returned to New York, where he underwent right hemicolectomy for an adenocarcinoma at the base of the caecum. Incidentally, the abdomen at hemicolectomy was entirely free of recurrent gastric cancer.

In order to treat cancer recurrence adequately it is imperative that patient follow-up be sufficiently frequent and thorough. There are surgeons who follow their cancer patients every few months, but many have their patients back far too infrequently, and then recurrence may be too advanced to permit of resection. There must also be sufficient time for a responsible man, not a junior, to take a careful history and carry out a thorough examination. It is essential to appreciate that the earliest indication of recurrence of growth may be given by mild symptoms and minimal signs, and these must be investigated as one would investigate a new case. In the absence of symptoms or signs, regular laboratory tests and *x*-ray examination should be carried out from time to time, so that recurrence is detected early enough. Admittedly, treatment of cancer to-day leaves much to be desired, but the optimistic attitude of Messrs. Cronin and Ellis is refreshing.—I am, etc.,

Liverpool, 8. REUBEN SILBERMAN.

Spontaneous Rupture of Tongue-tie

SIR,—Tongue-tie as a cause of symptoms has been described as a myth of hoary antiquity.[1] It has rightly been stressed that a fraenum which allows the tip of the tongue to protrude beyond the teeth or gums is long enough, and that a short fraenum grows longer and never interferes with speech. But it is probably wrong to suggest that, however short or tight the lingual fraenum may be, it will never cause symptoms. When a baby "sucks" the tongue is normally protruded over the lower gum. This can be seen whenever an infant is fed, and has been elegantly demonstrated cineradiographically by Ardran *et al.*[2] Tethering the tongue to the floor of the mouth might therefore interfere with the normal mechanisms of fixing on the breast and sucking. Below is reported a case in which a tight fraenum ruptured spontaneously during sucking.

Baby T. was born three weeks prematurely, weighing 4 lb. 11 oz. (2.2 kg.). The lingual fraenum was noticed to be tight at birth. He was put to the breast from the first day and sucked fairly well, but complementary feeds were needed until the 12th day to achieve a satisfactory weight-gain. Thereafter he was entirely breast-fed, but gained weight slowly. On the 15th day, while at the breast, he gave a sudden cry and stopped feeding. A small amount of bright blood was seen in his mouth. Closer examination showed that the tight fraenum had torn and the tongue could now be protruded beyond the gum.

Subsequently this baby remained a slow feeder, even when put on to artificial feeds at the age of 5 weeks. There is therefore no evidence that he was disabled by his tongue-tie. Nevertheless this incident shows that a short lingual fraenum is subjected to considerable tension when a baby feeds at the breast. Although this baby sucked reasonably well, a few babies with tongue-tie seem to have difficulty fixing on the breast. The indiscriminate snipping of tied tongues is very properly shunned, but it would be just as reprehensible to withhold "operation" from the occasional infant whose short fraenum is creating mechanical difficulties.

I am grateful to Mr. G. F. Gibberd and Dr. R. C. Mac Keith for permission to describe this case.—I am, etc.

Department of Child Health,
Guy's Hospital, S.E.1. R. W. SMITHELLS.

REFERENCES

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2 Ardran, G. M., Kemp, F. H., and Lind, J., *Brit. J. Radiol.*, 1958, **31**, 156.

Nasal Drops

SIR,—In the commonly recommended method of inserting nasal drops the patient is told to lie with his head over the edge of a bed. To anyone who has tried this it is soon clear that unless the neck is hyperextended (a position which is uncomfortable and difficult to achieve), the drops run along the floor of the nose into the naso-pharynx without reaching the upper nasal cavity.

A simple and more satisfactory method is described below for the treatment of acute or chronic sinusitis, using, in addition to decongestant drops, a solution of dequalinium chloride ("dequadin") which has been shown to have a wide spectrum of activity against Gram-positive and Gram-negative bacteria and some fungi, and is not inactivated by serum.[1] It has also been shown[2] that it does not interfere with ciliary action in quite high concentration.

Dequadin nasal drops are not yet available, but a solution made by dissolving one dequadin lozenge in four drachms (14 ml.) of boiled water has been found satisfactory and non-irritant when used as nasal drops in a large number of patients treated in the last 18 months.

The following method is employed: The patient is issued with decongestant drops ("tuamine" or "neophryn" have been preferred), 20 dequadin lozenges, and a 4-drachm (14-ml.) nasal drop-bottle.

The patient sits on a chair and bends forward with his head right down between his knees, so that the opening of the nostrils is upwards. The decongestant drops are inserted into both nostrils while the patient sniffs gently. While in the same position, the nose is pinched firmly to close both nostrils. The patient then attempts to sniff, giving a series of short, hard sniffs for one or two minutes. The head is then raised and the nose blown. The same procedure is repeated, using enough dequadin drops to fill the nostrils, until the discharge becomes clear.

The whole routine is repeated every 2–4 hours during the day. Sniffing between insertion of drops should be avoided as much as possible; when there is a desire to sniff or blow the nose, the patient should first bend down, pinch his nose, and sniff.

The procedure described above is also useful when used prophylactically at the beginning of a cold, especially if the patient is prone to sinusitis. The position employed is also used with advantage when inserting antihistamine or steroid drops for allergic rhinitis, ensuring far better distribution in the nasal mucosa than the method of lying over a bed, which is usually advised, or the use of a spray.—We are, etc.,

E. A. HAMILTON.
W. S. HAMILTON.

Oxford.

REFERENCES

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2 Banks, L. L., 1958, personal communication.

Hospital Decoration

SIR,—G. K. Chesterton stated that when lying in bed all he required to complete his happiness was a pencil long enough to enable him to draw on the ceiling. One of my own happiest childhood memories is of the pleasure to be derived when lying in bed from gazing at the wallpaper, which in those days invariably consisted of bunches of pink roses printed in regular lines over the whole wall. One could see them in lines—horizontal, vertical, and diagonal, and zigzag—and one could then join the zigzags to form squares, diamonds, and other geometrical shapes in almost limitless variety. I do not remember any of the pictures that may also have been hanging in their frames on the walls.

With these thoughts, and mindful of the need to have something to look at when lying in bed, I write to ask those who are lucky enough to be concerned with the design of children's wards in hospitals to prevent those whose business it is from decorating the walls with pictures or friezes which are merely representational, and to persuade them to go in for some modern abstract or near-abstract decorations.

It is my belief that once you have identified on the wall Mickey Mouse, Noddy, or the Cow Jumping over the Moon, and have made up your mind what they are doing, you lose interest in them, and in a very short time will cease to notice them, so that they might just as well not be there at all. On the other hand, abstract or nearly abstract pictures of the type painted by Picasso, Braque, and Kandinsky provide the bed-ridden patient with an unending focus of interest. He can of course try to guess what the pictures are meant to be. This approach alone will last him all his time in hospital, because you can be sure he will never find the answer. But he can also enjoy the colours, the shadows, the shapes, and the lines, and of these he will never tire.

Children's experience is very limited, and because of this many pictures which to an adult are purely representational are to the child viewer just as "abstract" and puzzling as many modern paintings and sculptures are to an adult. Children, being free from prejudice (that child of experience), have a far greater chance of enjoying what is offered for enjoyment by the non-representational artist.

Two further advantages of the non-representational picture are that, unlike Christopher Robin and, doubtless, in due course, Noddy, they do not date, nor do they carry with them the danger of being regarded by the scornful 10-year-old as "cissy." It should therefore be easier to persuade the committee to spend money on decorations which would safely be regarded as permanent and could accordingly be built into the walls for good and all. Down with Noddy and up with Picasso in paediatrics!—I am, etc.,

London, S.E.26. JOHN H. BURKINSHAW.

Chloroquine in Rheumatoid Arthritis

SIR,—Dr. R. R. Merliss (*Journal*, December 27, p. 1595) has commented on our article in the *Journal* of November 15 (p. 1199). We agree with him that a "multiplicity of drugs" has been used in rheumatoid arthritis, and that most of them gave indifferent results. Dr. Merliss appears, however, unaware that the literature on the therapeutic effect of chloroquine referred to well over 1,000 patients, that a "controlled study of untreated patients" compared with those on chloroquine has already been carried out by Rinehart,[1 2] and that we ourselves "were quite sceptical about any possible benefit" by chloroquine at the onset of our trials. These points have been totally overlooked by Dr. Merliss when he dealt with our paper.

Dr. Merliss's general remarks on the psychological basis of doctor-patient relationship require some comment. We can assure him that it has been our endeavour to mete out "enthusiasm and friendliness" in equal measure to all patients under our care. There have at no time been any preferential measures, psychological or otherwise, for the patients who have been reviewed in our paper. We cannot believe that Dr. Merliss really suggests that "enthusiasm and friendliness" should be denied to patients with rheumatoid arthritis in order that the benefit of a drug could be assessed more objectively.

We were pleased to read that Dr. Merliss agreed at least that chloroquine is free of serious toxic side-effects. We can assure him from considerable experience that the risk of transfusions causing homologous serum jaundice is very slight. If jaundice should occur it may indeed benefit the disease process of rheumatoid arthritis in the same way as infective hepatitis does. Lastly, we would be interested to know whether Dr. Merliss's criticism has been based on unfavourable results of his own trials.—We are, etc.,

H. FULD.
L. HORWICH.

Liverpool, 1.

REFERENCES

[1] Rinehart, R. E., *Northw. Med. (Seattle)*, 1955, **54**, 713.
[2] —— Rosenbaum, E. E., and Hopkins, C. E., ibid., 1957, **56**, 703.

Properties of Actal

SIR,—Our attention has been drawn to the comments of your expert contributor regarding "actal" in "To-day's Drugs" (*Journal*, December 13, p. 1471).

The active ingredient (sodium polyhydroxyaluminium monocarbonate hexitol complex) of this preparation was recently described and evaluated by us.[1] We realize that your expert's comments were probably written before our published work was generally available, and through the courtesy of your columns we feel it desirable to bring certain points to his attention. There is no justification for describing sodium polyhydroxyaluminium monocarbonate hexitol complex as a preparation of aluminium hydroxide. The two compounds have different physical and chemical properties. Our *in vitro* studies have shown that sodium polyhydroxyaluminium monocarbonate hexitol complex is markedly superior to the "ordinary *B.P.* tablet of aluminium hydroxide" in rate and amount of acid neutralized and in maintaining the *p*H of simulated gastric juice within the optimum *p*H range. Furthermore, available preparations of dried aluminium hydroxide gel vary greatly in their reactivity, even though complying with the official monographs.—We are, etc.,

J. R. GWILT.
J. L. LIVINGSTONE.
A. ROBERTSON.

Winthrop Laboratories Ltd.,
Newcastle upon Tyne.

REFERENCE

[1] Gwilt, J. R., Livingstone, J. L., and Robertson, A., *J. Pharm. Pharmacol.*, 1958, **10**, 770.

Inorganic Arsenic

SIR,—Dermatologists have good cause to be well aware of the dangers of arsenical treatment to which Professor A. V. Neale calls attention (*Journal*, December 27, p. 1593). Although there are occasional disasters, arsenical cancers of the skin are usually recognized in an early stage and treated successfully. Sommers and McManus[1] have drawn attention to arsenical cancers in the mouth, the oesophagus, upper respiratory tract, and in the renal tract, where they may not be diagnosed and treated so early.

Liquor arsenicalis is consequently not very much used by dermatologists nowadays; this is because of its known dangers and not necessarily because it is thought to be therapeutically ineffective. I have little doubt of its good influence in some cases of psoriasis and of dermatitis herpetiformis. The carcinogenic effects of arsenic are sometimes seen after relatively small doses given over a comparatively short period, and there is clearly a great deal of individual variation. Nearly always, however, there is a considerable lapse of time, and for this reason there are occasional cases where treatment with arsenic may be justified in elderly patients.

For these reasons one would hardly like to see arsenic completely abolished, though it should no doubt be used with great care and in very few selected cases where other treatment fails.—I am, etc.,

F. RAY BETTLEY.

London, W.1.

REFERENCE

[1] Sommers, S. C., and McManus, R. G., *Cancer*, 1953, **6**, 347.

POINTS FROM LETTERS

Addiction to Unrestricted Drugs

Drs. S. J. MINOGUE and F. J. KYNEUR (Sydney, Australia) write: It has been our experience in Sydney that addiction to unrestricted drugs, such as carbromal, "persomnia," chloral hydrate, aspirin, and many others, is far more common than is usually realized (see the article by Drs. C. P. Seager and A. R. Foster, *Journal*, October 18, p. 950, and subsequent correspondence). Even the new tranquillizers, such as chlorpromazine and others, become drugs of addiction. Each one, too, may cause a form of chronic poisoning which is recognizable clinically. However, the usual clinical picture to-day is subacute poisoning caused by a number of drugs. The patient is sleepless, and takes probably one of the barbiturates, or carbromal, as a hypnotic. Next morning he is, in the Australian vernacular, "dopy," and must take a stimulant, usually one of the amphetamine preparations, to enable him to face the day's work. Then, because he becomes over-stimulated mentally, he must take a tranquillizer, such as chlorpromazine or carbromal, to steady him down. A vicious circle is soon established. The doses and frequency with which the drugs are taken are rapidly increased, and acute or chronic poisoning is a very common result. The acute poisoning is manifested by restlessness, insomnia, and fears and hallucinations of very great impending harm. The condition is commonly diagnosed as acute mania, and treated by E.C.T., which makes the symptoms more acute. Or it may be treated by large doses of tranquillizers, which simply add to the toxaemia present and make the condition worse. Such conditions were wellnigh unknown 30 years ago. They are but a complication of physical methods of treatment in psychiatry—the treatment of symptoms and not of diseases. In such cases one reverts back to the old-fashioned and out-of-date treatments of 30 years ago—withhold sedatives and saturate the patient with fluids, two or three gallons (9–13.5 litres) a day. The improvement is rapid, and the patient avoids all the complications of modern treatment, the loss of memory after E.C.T. and the necessity for large doses of tranquillizers "to keep him on an even keel." In the chronic form of poisoning, the patient is depressed and is commonly diagnosed as having "a depressive reaction." But the face betrays the type of drug to which he has been addicted—the Parkinson mask of chlorpromazine addiction, the peculiar bluish tint of those taking large doses of aspirin, the peculiar redness in depth of those poisoned by reserpine. Again the treatment is not by E.C.T., which tends to perpetuate it, but the old-fashioned elimination methods. These give excellent results, without any deterioration of the mental functions. It is curious, too, that many of these patients are alcoholics, who follow a classical clinical course of alcoholism. Such patients are much more common in Australia than in London and Europe.

Obituary

J. C. GREGORY, M.R.C.S., L.R.C.P., D.Obst.R.C.O.G.

Dr. J. C. Gregory, chairman of the All England Lawn Tennis Club, Wimbledon, and a former Davis Cup player, died in the dressing-room of the club on January 10, just after he had finished a doubles match. He was 55 years of age, and had been in practice in Hemel Hempstead for nearly 25 years.

John Colin Gregory was born at Beverley, Yorkshire, on July 28, 1903, the son of Dr. W. H. Gregory. From Rossall School he went on to University College Hospital as a medical student, and qualified M.R.C.S., L.R.C.P. in 1928. After holding a number of house appointments at U.C.H., he settled in general practice at Hemel Hempstead, Hertfordshire, in 1934, and two years later obtained the Diploma in Obstetrics of the Royal College of Obstetricians and Gynaecologists. In addition to the work of his practice he held appointments at the West Herts and St. Paul's hospitals at Hemel Hempstead, being medical superintendent of the latter hospital. He was chairman of the West Herts Division of the British Medical Association from 1948 to 1950.

[*Universal Pictorial Press and Agency*

Dr. Colin Gregory was one of the best lawn-tennis players this country has produced. Tennis was in his blood, for his mother was the first lady champion of Yorkshire, and the youngest. He won the North of England boys' singles in 1919 and 1920, and the Yorkshire singles championship in five successive years (1923–7) and again in 1930, 1931, and 1949. He was six times on the winning side in the county's men's doubles championship and four times in the mixed doubles. He first represented England in 1926, when, as a member of the Davis Cup team, he played against Spain and France, and he continued to be an England choice until 1930. In 1929 he was ranked (with H. W. Austin) No. 1 in England, and was the first Englishman to be seeded at Wimbledon. In that year he won both the Australian and Scottish championships, and he and I. G. Collins reached the final in the men's doubles at Wimbledon; the same pair reached the semi-final in 1930. From 1949 to 1953 he was the non-playing captain of the British Davis Cup team, and in 1952, at the age of 49, decided to partner A. J. Mottram in place of the injured Geoffrey Paish in the doubles match against Jugoslavia, which the British pair won. In recognition of his outstanding services to the game, leadership in the Davis Cup, and initiative at Belgrade in 1952, he was presented with a special award by the Lawn Tennis Writers' Association. In that year he was president of the Yorkshire Lawn Tennis Association. After giving up the captaincy of the British Davis Cup team, Dr. Gregory became vice-chairman of the All England Club, and in 1955 was elected chairman. Although lawn tennis was his first choice as a game—and he played it always as a game—Colin Gregory was a natural ball player. In 1930 he tied with H. A. Sabelli in the lawn-tennis golf foursomes; he represented Yorkshire at squash rackets, and in 1931 won the North of England championship; and he represented University College Hospital at Rugby football and cricket, as well as at golf and squash rackets.

Dr. Gregory leaves a widow, one son, and two daughters.

J. G. A. G. writes: Colin Gregory was a family doctor. He was no frustrated specialist who had slipped from "the ladder." The son of a general practitioner of the highest quality, he set out deliberately to equip himself for the work of general practice. His career as a resident at U.C.H. bears testimony to the single-mindedness of his purpose. He was successively H.P. to the medical unit, H.S. to the surgical unit, H.S. to the late Clifford White, and finally R.M.O. To each of these appointments he gave all his energy and drive and came out the richer in experience. I first got to know him when he was R.M.O. and I was a final-year student. When he took out-patients in the absence of one of the physicians he had much to teach about the ordinary things of medicine—the practical and the homely things. He endured our efforts with genial patience, never once making us feel our ineptitude nor mocking our mistakes. At the end of my job as H.S. to the obstetric unit in 1936 I was visited one day by Colin Gregory, who came to me on the suggestion of Dick Sloley, to ask if I would be interested in general practice in Hemel Hempstead. That began an association which has now been ended by his tragic death at the All England Club, which he loved and served so well.

Although I knew "Greg" well for 23 years, I am still wondering what was the driving force behind the man. No one can estimate the amount of work that Gregory could get through or where he found all the time to do the many things he did in addition to his routine daily work. It would seem now that he was borrowing time from life itself. He was a man of strong convictions, and once his mind was made up it was difficult to persuade him to change it. Although a tall man and a strong one he was amazingly gentle. Children adored him and had absolute trust in him, and I can speak from personal experience of the kindness and comfort he brought to patients in pain or sorrow. His mere presence was enough to allay fear and his strength to promote confidence.

Gregory's greatest single contribution to Hemel Hempstead was in the maternity unit of St. Paul's Hospital. In 1939 the old Hempstead House — "The Institution"—was taken over by University College Hospital and he was appointed medical superintendent, a post which he filled throughout the war. When, midway through the war, U.C.H. vacated the "base hospital," as it had become, "Great Ormond Street" took over. In 1946 the Hospital for Sick Children returned to London, leaving behind the altered buildings quite empty. With great foresight and tenacity Gregory persuaded the Hertfordshire County Council to establish a maternity unit with a potential of 54 beds in the now renamed St. Paul's Hospital. The entire planning of equipment, and structural alterations then and since, were the work of Colin Gregory, and the whole evolution of the unit is a monument to him. What this cost him in time and energy can hardly be guessed, but we know that he dashed here, there, and everywhere to get the best advice—this while running a most successful general practice. His list of public appointments alone was formidable, apart from the number of insurance companies for which he performed life examinations. He even found time to attend the Law Courts on two occasions to give a general practitioner's opinion on behalf of colleagues whom he did not know but who were being assailed by litigious patients.

There must be many many people, rich and poor, whose lives have been enriched by contact with this striking, dynamic figure. The gloom which descended over Hemel Hempstead at his death was not confined to his own patients but was widespread. For Hemel Hempstead was proud of its J. C. Gregory. Neither in the big world of international lawn tennis nor in the smaller world of his practice will he be quickly forgotten. A loyal and devoted son of U.C.H., he has shed lustre on his hospital and medical school and can fairly be ranked as one of the greatest all-rounders the hospital has ever known.

Colin's family, whom he adored and who worshipped him, must find a great measure of comfort in their loss in the

wealth of sympathy which is even now converging upon them from all corners of the world. For everyone who knew him recognized his stature and feels a personal loss.

SIDNEY RIDDIOUGH, M.B., F.R.C.S.

Mr. Sidney Riddiough, honorary consulting surgeon to Addenbrooke's Hospital, Cambridge, died at his home at Cambridge on January 7. He was 67 years of age.

Born on September 21, 1891, Sidney Riddiough was the son of Mr. J. T. Riddiough, of Bradford, and was educated at Bradford Grammar School and King's College, Cambridge, where he was an exhibitioner. Having obtained honours in the Natural Sciences Tripos in 1912 and in the Mathematical Tripos in 1913, he became master at the Leys School, but shortly afterwards he decided to study medicine at Guy's Hospital. Qualifying in 1917, he graduated B.Chir. in 1918 and M.B. in 1919, and became a Fellow of the Royal College of Surgeons of England in 1931. After qualification he held the appointments of out-patients officer at Guy's Hospital and house-physician at Addenbrooke's Hospital, Cambridge. After a period in the R.A.M.C. he returned to Guy's to become chief clinical assistant in the department of neurology. In 1923 he entered general practice at Dewsbury, Yorkshire, joining the staff of the General Infirmary as an assistant surgeon. When he left Dewsbury in 1931 he was appointed honorary surgeon to the infirmary. In the following year he settled in practice in Cambridge, where he remained for the rest of his life. As his surgical work developed he tended to specialize more in urology and venereology. Many hospitals in the neighbourhood had the benefit of his services: he was consulting surgeon to Huntingdon County Hospital, consulting urologist to Peterborough Memorial Hospital, surgeon at the Royston Cottage Hospital, and consulting surgeon to the United Cambridge Hospitals. He was a member of the Faculty of Medicine in Cambridge University.

A colleague writes: By the death of the well-known and beloved consulting surgeon Mr. Sidney Riddiough, a wise and kindly friend has been lost to a wide circle of men and women in all walks of life both in Cambridge and elsewhere.

Mr. Riddiough was a bachelor. Of a genial disposition, a charming host, and a man of wide reading, he was also an after-dinner speaker and raconteur of considerable note and ability. Active in public life, he was at one time a member of the council of the borough of Cambridge, and also a member of the Cambridgeshire county council. In freemasonry he held the rank of deputy provincial grand master of Cambridgeshire, and was past grand deacon of England. In his earlier days in Yorkshire and later when he came south he was a keen hunting man. For many years a member of the Cambridgeshire Harriers, he was well known to point-to-point enthusiasts—particularly at Cottenham, where his services as honorary medical officer were so much appreciated. He was keenly interested in shooting, and was well known as a good shot; and as an active angler trout fishing was one of his most enjoyed pastimes. He was president of the Rodney Dramatic Club, Cambridge, for twenty-one years, the longest tenure of that office in the sixty years of its history. A sick man for some time, he had borne a worsening illness with fortitude and gallantry. His passing will be sadly mourned.

J. C. H. BROWNE, M.R.C.S., L.R.C.P.

Dr. J. C. H. Browne, medical superintendent of the Cunard Steamship Company, died suddenly in Liverpool on January 9. He was 48 years of age.

James Charles Haines Browne was born in 1910, the eldest son of the late Dr. Charles Haines Browne, of Southsea. His family was Anglo-Irish, and since 1800 every generation has given male members to the medical profession. Besides his father and grandfather, five of his uncles were also doctors, and his two younger brothers are both doctors: one is in Ghana, and the other is medical officer of health to Chichester City and Bognor Regis.

M. P. B. writes: From Portsmouth Grammar School Jim Browne went on to the Middlesex Hospital, qualifying in 1934. After holding house appointments at St. Mary's Hospital, Portsmouth, he went to sea for one trip only, but, having a grandfather who had been a seafaring commodore, he found that the sea was in his veins also. He joined the Cunard Steamship Company in 1936, when he was appointed ship surgeon in the *Antonia*. Until the outbreak of the war he was on the Montreal, New York, and Nassau runs, and he was surgeon to the *Lancastria* until very shortly before she was sunk with heavy loss of life in 1940. He was in New York for about three months looking after the medical needs of the crews of the two *Queens* and the *Mauretania*, and when these ships become mobile he was posted to the *Mauretania*, in which he served for five years while she was troop-carrying. It was in this ship that he met his wife-to-be, when she was serving on special duties as a Wren officer. In 1946, at the age of 35, Jim Browne became medical superintendent of the Cunard White Star Line, and he made many improvements in big-ship hygiene, benefiting all who travelled on the seas. He had never been ill in his life, and he came from a long-lived family, and his death at the early age of 48 from coronary thrombosis is a signal of his devotion to duty.

He leaves a widow, to whom the sympathy of all his many friends will be extended.

NOAH PINES, M.B., L.M.S.S.A., D.O.

Dr. Noah Pines, who was in general practice at Stepney and was formerly ophthalmic registrar to the London Jewish Hospital, died at his home in north-west London on January 10. He was 71 years of age.

Noah Pines was born in Moscow on February 15, 1887. He received his medical education at the Imperial University, Kieff, graduating M.B., with honours, in 1911. During the first world war he served as a senior medical officer with the Russian Army. For his war services he was appointed a Chevalier of the orders of St. Stanislas and St. Anna of Russia, and of the Crown of Belgium. After the war he left Russia for England, and obtained the diploma of L.M.S.S.A. in 1920. He settled in general practice at Stepney, in London, but he always had a special interest in ophthalmology and served the London Jewish Hospital for many years in that specialty. He took the Diploma in Ophthalmology of the English Royal Colleges in 1951. He was chairman of the Tower Hamlets Division of the British Medical Association in 1956–7.

A. H. L. writes: Noah Pines was trained as an ophthalmic surgeon by his uncle, who was ophthalmic surgeon to one of the hospitals in Kieff, in the Ukraine. Starting in general practice in Stepney after the first world war, he soon had a large number of patients, but his heart remained in ophthalmology and he became clinical assistant and, subsequently, registrar in the ophthalmic department of the London Jewish Hospital. He worked in that department for the rest of his active life and was much liked by the staff and patients. In fact it may be said that he became identified with and constituted one of the principal supports of ophthalmology in that hospital. During the second world war he carried on the work of the department single-handed, in addition to his work as divisional surgeon of the St. John Ambulance Association and surgeon to the civil defence force. This latter work, in view of the heavy bombing of his part of London, was especially arduous. Through it all he retained his equanimity and never shirked any duty. He was an original thinker, and his work on retinal vascular disease was very valuable. He was an expert on trachoma, and his operative technique was of a high order of excellence. He had a charming disposition and will be sadly missed by a large circle of friends.

V. K. DRENNAN, M.Ch.Orth., F.R.C.S.Ed.

Mr. V. K. Drennan, consultant orthopaedic and traumatic surgeon to the Clwyd and Deeside Hospital area, died at the Northern Hospital, Liverpool, on December 19, 1958. He was 47 years of age.

Vernon Kent Drennan was born in Liverpool on January 18, 1911. He graduated M.B., Ch.B. from Liverpool University in 1935 and then held the posts of house-surgeon at the Stanley Hospital and resident medical officer at Walton Hospital, Liverpool. He next entered the school medical service. In July, 1939, he joined the Territorial Army as regimental medical officer to an anti-tank regiment, and during the second world war served in Malaya, India, and Burma, first as surgeon to a casualty clearing station and later as surgical specialist in charge of a mobile surgical unit. He saw much active service with the 14th Army. After the war he was appointed resident surgical officer at Walton Hospital, Liverpool, and in 1948 he obtained the F.R.C.S.Ed. Realizing that his main interest was in orthopaedic surgery, he then transferred to the Bootle General Hospital as orthopaedic registrar, and in 1950 was successful in the M.Ch.Orth. examination at Liverpool. The following year he was appointed to the post of consultant orthopaedic and traumatic surgeon to the Clwyd and Deeside Hospital area, where he soon established a very extensive and very successful orthopaedic hospital service and a busy private practice.

Always a keen Territorial Army officer, he joined the 8th (Liverpool) General Hospital, R.A.M.C.T.A., when it was reformed in 1947. His first appointment was as surgical specialist; later he was promoted to lieutenant-colonel in charge of the surgical division, and in 1955 he assumed command of the hospital with the rank of colonel.

P. R. H. writes: Vernon Kent Drennan was very happy in his work, for orthopaedic surgery had always fascinated him. He was a great enthusiast and a very capable and tireless worker, and his untimely death leaves a gap which will be difficult to fill. He leaves behind a host of friends, for he had the great gift of making friends wherever he went. He was welcome in any company. Essentially an optimist, with wide interests, he was a good conversationalist and an excellent raconteur, a great lover of music, and a first-class pianist. He had little time for leisure, but was a skilful and successful angler, and perhaps an occasional day on the river brought him most pleasure.

His Territorial Army hospital was very close to his heart. It involved heavy calls on what little time he could spare, but of this he gave unstintingly; he rarely missed a parade. He found time for weekend exercises, and even as late as last summer went to camp as usual. This must have proved a tremendous tax on his waning physical powers, but he did not show it, and it was one of the most successful camps in the history of the unit. About three years ago the first evidence of the long illness which could only prove fatal came to light. Although he well knew the prognosis, he refused to allow this to interfere with his work or with his family life. Despite failing health and for the last year supported alone by transfusions at ominously decreasing intervals he carried on with his work until a few weeks before his death. To the end he remained cheerful, courageous, and full of gratitude to the doctors and nurses who had the privilege of caring for him. Our deepest sympathy is extended to his widow and his two young children.

D. W. B. writes: May I add this small tribute on the passing of a very dear friend? Vernon Kent Drennan was a fascinating personality, with a whole-hearted love of life and people. An evening with him and his wife was always a great pleasure—often the main dishes, of Indian origin, being cooked by himself. The conversation would always be stimulating and cover a wide range of interests. He was wont to say that his would be a "short life and a merry one," and he certainly lived it to its full. I am glad that he with his wife had the great honour and pleasure of being presented at a Garden Party at Buckingham Palace in 1957 and of being an invited guest at the Trooping of the Colours in that year. We have sustained a grievous loss, and our heartfelt sympathy goes to his widow and the two children.

W. R. THOMSON, M.B., Ch.B.

Dr. W. R. Thomson, who practised in Stanley, Co. Durham, died in hospital at Shotley Bridge on December 30, 1958, at the age of 43.

William Russell Thomson was born near Glasgow on April 12, 1915, and graduated M.B., Ch.B. at Glasgow University in 1944, thereafter holding resident appointments at Ruchill Hospital and the Victoria Hospital, Glasgow. An outstanding athlete, he was university heavyweight boxing champion, a member of the university golf team, and narrowly missed being capped for Scotland at Rugby. He played in the South of Scotland area golf team from 1948 to 1952.

W. J. writes: Bill Thomson began practice in Stanley in 1953, and during the next five years endeared himself to his patients and colleagues alike by his conscientious, perhaps too conscientious, devotion to duty, often in the face of painful ill-health. His circle of friends was indeed wide, for he won the Durham county golf championship in 1955 and played regularly for the county team up to the time of his sudden death. He was the ideal companion, both on the golf course, where his skill and courteous demeanour were greatly admired, and elsewhere, and at all times his cheerful and engaging personality made him wonderful company. During the last few years of his life he endured two major operations and a previous attack of coronary thrombosis. It was characteristic of his personal courage that he carried on his many activities with all his normal enthusiasm, and practically on the eve of his death was preparing to celebrate Hogmanay with typical Scottish fervour. The final attack of coronary thrombosis came at 5 a.m. on December 30, and his extraordinary fortitude can best be judged by the fact that he attempted to dress in order to conduct his morning surgery before being admitted to hospital. His tragic and untimely death removes an outstanding personality from his many friends in the area, and is an irreparable loss to his wife and two daughters, to whom we extend our deepest sympathy.

J. W. McDONALD, M.B., Ch.B.

Dr. J. W. McDonald, who was in general practice in Edinburgh for thirty-five years, died at Edinburgh Royal Infirmary on December 20, 1958, at the age of 67. He had been ill for three months.

James Walter McDonald was born on May 28, 1891, the son of the late Dr. James McDonald, of Motherwell. A medical student at Glasgow University, he graduated M.B., Ch.B. in 1913. He served in the R.A.M.C. in the first world war until 1919, being wounded in 1917. After his return to civilian life he was in practice at Lochmaben, Dumfriesshire, until 1923, when he moved to Edinburgh, where he remained in the same practice until he retired last October. He leaves a widow, two daughters, and a son, who is in practice at Wensleydale, Yorkshire.

E. S. CURTISS, M.B., B.S., F.F.A. R.C.S.

The obituary of Dr. E. S. Curtiss was printed in the *Journal* of January 3 (p. 53).

E. G.-E. writes: As the weeks pass by it becomes increasingly difficult to believe that Dr. E. S. Curtiss is no longer working with us at the Miller General Hospital. Colleagues have already referred to his many achievements. His friendship was my privilege for a quarter of a century. I would like to place on record his love of humanity. Stuart was a humanist. He was also a born anaesthetist.

His charming personality and his wide experience of clinical medicine inspired his patients with peace of mind and a feeling of bodily security. His modesty and his knowledge of surgical problems imbued the operator with strength of purpose in the management of a difficult case. His movements in the operating theatre were unobtrusive and methodical; he was discreet at all times and never in a hurry. The care of the patient and the wishes of the surgical team were always uppermost in his mind. He was a delightful companion and a generous host. He was devoted to his friends; they rallied round him and his family in his illness. His infinite capacity to enjoy life was matched by his uncomplaining courage in facing its inevitable termination. There is a deep sense of personal loss here at the Miller Hospital. To his widow and his two daughters we offer our deepest sympathy.

Medical Notes in Parliament

PROSPECTS FOR THE LAST SESSION

Parliament has resumed this week, after the Christmas recess, what is likely to be its last session before a general election. Apart from the alarms and excursions of foreign affairs, its remaining work will be devoted chiefly to finance and social reform. An early dissolution—and the end of the "winter," during which there will be no election on the Prime Minister's repeated promise—would interrupt both. Such a foreclosure would mean delay, but not loss, to much of the social legislation. Although the prospective reforms are not wholly accepted by all reformers, some of whom seek to reach much the same ends by rather different means, they are at least not in the party cockpit, and much of the work that had been done on them could remain to serve as the basis of the next round, even if the parties should by then occupy different corners.

Mental Health Reform

Foremost in this work of reform is the Mental Health Bill, already assured of a wide acceptance since its contents were published on January 6, and waiting for second reading. This may well not happen until mid-February. It is probably intended that it shall be out of the Commons well before Whitsun, when the Finance Bill and the Estimates will be making heavy inroads into Parliamentary time.

Two factors can account for the time-lag before the second reading. One is that the Pensions Bill, being the most contentious of the social legislation in prospect, is likely to be put on the stage first. The second lies within the Bill itself. A large part of the burden involved in applying modern concepts to the care of the mentally disordered will fall on the local authorities, and will be costly. Consultations between the Government and the authorities are still continuing, and may take some time. The effort to return many of the mentally ill to community care entails the provision of hostels and homes, and the failure to make this duty mandatory (as the Royal Commission proposed) and to ensure that the necessary capital is available is viewed with critical disappointment.

Apart from this, most attention is likely to be attracted to the proposals for compulsory treatment and the definition of psychopathic disorders. Not only those who regard the definition as too narrow will put forward what they regard as attempts to improve it. Compulsory treatment, even in the greatly restricted categories now envisaged, still evokes the major issue of personal liberty. The disappearance of the lay magistrate will not pass without expressions of regret, even of disapproval; on the other hand, the requirement that, of the two medical recommendations needed before compulsory powers can be used, one must be signed by a doctor with special experience in the diagnosis and treatment of mental disorders has gone a long way to allay other objections.

Industrial Legislation

Social reforms now engaging Parliament's attention have of course a much wider scope. They cover such diverse affairs as the old and familiar topic of health and safety rules in factories and the new and (to some) frightening dangers of nuclear installations.

The Factories Bill, introduced without the companion piece for office workers based on the Gowers Report, is in standing committee. The Nuclear Installations (Licensing and Insurance) Bill has passed through the Lords. Weighted as it is by emotion and international politics, the Bill is likely to receive much rougher treatment in the Commons, where the demand for the removal of the time limit on claims will be renewed.

Still in the course of preparation are the Home Secretary's plans for penal reform, expected to be ready for publication some time in February.

Drugs for Private Patients

A topic recurring at irregular intervals in the public press is the provision of drugs for private patients. The B.M.A. committee's proposal has already attracted a critical rejoinder in one area (Birmingham), where the Labour M.P.s have been briefed on their views.

With an expanding economy and the prospect of an "easy" Budget the pressure for abolishing the prescription charges is likely to increase. Sir Frank Newsam's report on the role of the family doctor in the Health Service is likely to prove another fruitful source of probing questions to the Minister of Health. And away in the dim distance that shrouds an autumn general election lies concealed the final and long-delayed report from the inquiry into doctors' pay and remuneration — and, more important, the Government's decision on the action to be taken about it.

Medico-Legal

"MERCY KILLING" SENTENCE REDUCED

[FROM OUR LEGAL CORRESPONDENT]

William Ernest Moodie, a prison officer at Durham Prison, was found guilty of manslaughter at Durham Assizes last October on an indictment for murder to which his defence was diminished responsibility under section 2 of the Homicide Act, 1957.

Moodie's daughter was a congenital idiot. She could neither walk nor talk and was subject to terrible seizures without warning, so that her mother or father had to be with her all the time. Her parents had been given the hope that with care and attention they could bring her up practically as a normal child, but as the years went by it became apparent that this was impossible, and the family tragedy became worse and worse. Finally Moodie, when the child was 12, under extreme stress of emotion gave her a dose of "nembutal" (pentobarbitone sodium), to which he had access in the prison, and, while she was unconscious in bed, suffocated her. After writing a letter to his wife, Moodie gave himself up to the police.

In finding him not guilty of murder but guilty of manslaughter the jury made a strong recommendation for mercy. Mr. Justice Ashworth sentenced him to three years' imprisonment, and from that sentence Moodie appealed on the ground that the judge had not given full effect to the jury's recommendation or taken into consideration the full facts of the case.

The appeal was heard by the Court of Criminal Appeal on January 13 (*The Times*, January 14). In giving the judgment of the Court, the Lord Chief Justice, Lord Parker, said that Moodie was a man of exemplary character who was devoted to his family. If there was

only him to consider, sympathy would dictate the most lenient of sentences. But nothing that the Courts did should lead the public to believe that a killing of this kind was other than a grave offence. The circumstances of the case were, however, such that the Court felt they could reduce the sentence. Persons such as Moodie were not criminals in the ordinary sense, and often acted with what they considered were the best of motives. The real deterrent, if deterrent there were, was not the question of how many years' imprisonment they would get.

Moodie's sentence was reduced to one year's imprisonment.

FATAL BLOOD DONATION

An unusual accident, ultimately fatal, befell a blood donor at Koldby, Denmark, recently. He died suddenly, a month after a blood donation, as a result of the stylet from the taking needle entering and perforating the heart and so causing a haemopericardium.

Nothing to arouse suspicion that the stylet might have entered the vein occurred during the donation. At first the blood ran freely enough, but then it stopped. The needle was therefore rotated a little and pushed further into the vein, but, as this produced no improvement, the needle was withdrawn, a fresh puncture made, and the rest of the blood drawn off through that. The donor complained of nothing more serious than that the operation had been a little more painful than usual.

Several days later the donor complained of some pain in the arm. Examination showed what was taken for an aseptic phlebitis. Nearly four weeks after the donation he complained of dyspnoea on exertion. Two days later he was found dead in his car. At necropsy there was a thrombophlebitis of the distal portion of the brachial vein. The stylet was found in the right ventricle of the heart. One end was embedded in a papillary muscle, the other had perforated the heart and pericardium posteriorly. The pericardial sac contained about 200 ml. of blood.

We are indebted to Dr. Hvass Hansen, of Koldby, for this account.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

In Congregation on November 29, 1958, the degree of M.B. was conferred on Susan J. de Graaff-Hunter.

UNIVERSITY OF ABERDEEN

At a Graduation Ceremony on December 17, 1958, the following degrees were conferred:

M.D.—A. H. Emslie-Smith (with commendation).
CH.M.—G. F. Cassie.
M.B., CH.B.—M. Adam, Alison H. Carss, Dorothy P. L. Chua, A. M. Cowe, G. R. Dawson, I. A. Garden, W. G. Johnston, M. McA. Lees, Norna Mackay (née Pottinger), G. G. A. Middleton, R. Miller, J. S. S. Mowat, R. L. Renton, C. Y. S. Rettie, V. L. Tosh, A. V. R. Watson, A. S. Wiseman.

UNIVERSITY OF DUBLIN

SCHOOL OF PHYSIC, TRINITY COLLEGE

The following degrees and licences were conferred on December 11, 1958:

M.B., B.CH., B.A.O.—A. K. P. Bermingham, Elizabeth M. Bowden, Janet I. Byard, J. H. Chester, Heather G. M. Clarke, Monica M. Cronin, P. R. C. Dowse, Ruby S. Indar, Dolores King, F. G. H. Knight, D. R. Mandry, W. L. B. Miller, C. G. van R. Mostert, Cicely E. Newman, J. M. O'Brien, Gerdina B. Oosterhuis, R. D. Taylor, D. A. W. Williams, D. C. P. Yeo.
L.M., L.CH., L.A.O.—M. A. Lewis.

UNIVERSITY OF DURHAM

In Congregation on December 13, 1958, the following degrees were conferred:

M.D.—E. V. Cox.
PH.D. IN MEDICINE.—S. I. M. G. Mannan.
M.B., B.S.—G. D. Gale, D. McK. Gemmell, Evelyn P. Hardy, P. Hodgson, M. McKay, K. Matthews, O. C. Nwankwo, Ann E. Parker, S. R. Patel, Margaret M. Sanderson, Dorothy A. Watson.

UNIVERSITY OF LONDON

The degree of Ph.D. in the Faculty of Medicine was awarded to J. N. T. Gilbert on November 11, 1958, and to E. H. L. Harries, M.B., B.S., and I. Ll. Thomas on November 25.

The degree of M.D. was awarded by the Senate on November 19, 1958, to K. M. S. Hume.

The following candidates at the Institute of Psychiatry have been approved at the examination indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN PSYCHOLOGICAL MEDICINE.—W. H. Allchin, J. M. Hinton, N. B. Kreitman, S. Wolff.

The following have been appointed or nominated for appointment or reappointment as representatives of the University on the governing bodies of the institutions indicated in parentheses: Professor J. M. Mackintosh (London School of Economics and Political Science) for the year ending December 31, 1959; Dr. E. C. Warner (West London Hospital Medical School); Dr. S. Gnessen (Joseph Priestley and Mount Pleasant London County Secondary School); Dr. St. G. B. Delisle Gray (Upton House London County Secondary School); Dr. K. J. Gurling (Vauxhall Manor London County Secondary School).

UNIVERSITY OF MANCHESTER

The following candidates have been approved at the examinations indicated:

FINAL M.B., CH.B.—W. D. Ashworth, A. Aspinall, A. S. Buttoo, D. B. Case, W. G. Cautley, Freda M. Crossley, R. P. Davies, A. J. Ellison, P. J. Falconer, R. S. Goldberg, W. M. Gould, R. Greenbaum, Evelyn W. S. Harris, G. G. Hay, K. Haywood, D. S. Hopton, D. N. Hutchinson, J. K. Johnson, P. M. Keane, R. Lansdell, D. A. Leighton, P. M. Lenten, Freda M. Lord, D. Morrison, Joyce Newton (née Holgate), J. R. Norris, H. Pomfret, H. S. Radden, J. N. Roskilly, R. J. Roycroft, E. Shaoul, H. J. Shapiro, D. A. Thomas, J. Thompson, J. D. Wilson, P. R. Wood, Ann C. Wright.
DIPLOMA IN PUBLIC HEALTH.—H. Diggles.

UNIVERSITY OF WALES

At a Degree Congregation held on December 17, 1958, the following candidates were admitted to the degrees of M.B., B.Ch.:

C. B. Bissessar, E. G. L. Davies, H. C. R. Davies, A. H. M. El-Shaboury, S. L. Evans, Enid B. Griffith, Sylvia M. Harris, L. Henkel, Anne E. Jones, Margaret G. Jones, J. Lowther F. Navas, R. E. Needs, W. W. Sweet, B. L. Thomas, K. E. Young.

UNIVERSITY OF BIRMINGHAM

Dr. A. P. D. Thomson has been appointed representative of the University on the Birmingham Regional Medical Recruitment Committee for 1958–9, and Dr. J. H. Sheldon has been reappointed representative on the governing body of Bilston Boys' Grammar School.

The following have been appointed lecturers in the subjects indicated in parentheses: Dr. A. Glass and Dr. A. W. Rogers (Anatomy); Dr. J. D. Cumming (Physiology); Dr. H. A. Ellis and Dr. D. J. Parish (Pathology); Dr. S. H. Taylor (Medicine); Mr. F. Ashton and Mr. G. T. Watts (Surgery); Dr. E. M. Little (Obstetrics and Gynaecology). Dr. June K. Lloyd has been appointed Research Fellow in Paediatrics and Child Health.

Professor J. M. Smellie, Professor of Paediatrics and Child Health since 1946, retired on September 30, 1958.

The following lecturers resigned their appointments on September 30, 1958: Dr. J. Williams (Anatomy); Dr. R. F. Crampton and Dr. D. M. Matthews (Physiology); Mr. A. L. T. Easton (Obstetrics and Gynaecology); Dr. J. H. Edwards (Social Medicine).

In Congregation on December 12, 1958, the following degrees were conferred:

M.D.—D. F. Davies.
CH.M.—P. G. Bevan.
PH.D.—*In the Faculty of Medicine:* F. N. Garratt, J. F. Nunn.
M.B., CH.B.—B. H. Ackers, J. Ashton, R. M. Badminton, P. W. Burton, J. S. Coles, C. D. Dalby, J. T. Dennis, D. C. Dukes, A. Dunnill, E. E. Genever, D. A. Gibson, B. Henley, G. R. Horton, Danuta Kaczmarska, J. S. Levett, K. E. Luckman, Shirley M. Machin, R. F. Norris, T. J. Pearman, G. C. Rowe, A. J. R. Smout, G. B. Wolloff.

UNIVERSITY OF LEEDS

The following candidates have been approved at the examinations indicated:

M.D.—P. D. Roberts.
M.B., CH.B.—Gillian Gower (with second-class honours), R. L. Green (with second-class honours), Lucy D. Bird (with distinction in surgery), Mun Kam Chool, Jean Dawe, G. H. Farrington, A. E. Finnigan, D. F. Harrison, B. R. Harvey, Margot L. E. Jenkins, A. R. Johnson, H. Jordinson, T. Kay, W. E. Kirkpatrick, D. London, I. C. A. Martin, K. R. Peel, D. A. Penny, M. Priest, R. H. Raybould, S. S. Sanders, P. G. Tannett, R. Trigwell, D. Uttley, B. C. Uzodike, G. Wardell, Sonia M. Werba, M. A. Wilson.

UNIVERSITY OF BRISTOL

The following candidates have been approved at the examination indicated:

M.B., CH.B.—B. A. E. Chapman, M. B. Clark, Joan D. Clay, Valerie R. Cormack, G. D. Henley, Valerie C. Hughes, H. S. Lassey, R. Mapstone, B. R. S. McClements, R. K. H. Parker, P. C. Power, J. E. H. Shield, L. F. Webster. *In Group I, completing the examination:* A. H. Ogden, Glenaya S. Shute. *In Group II, completing the examination:* Anne P. Simon.

ROYAL COLLEGE OF SURGEONS IN IRELAND

On November 21, 1958, the Fellowship of the Royal College of Surgeons in Ireland was conferred on D. M. McNab.

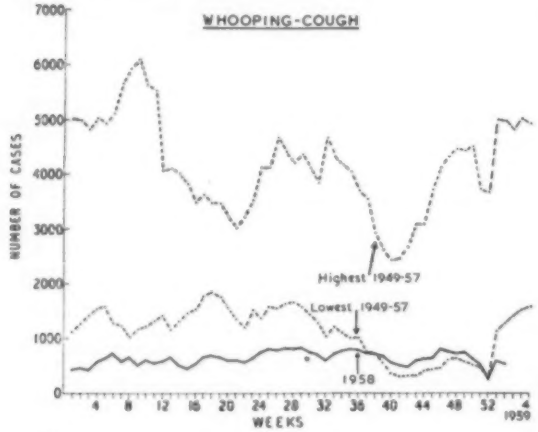
Vital Statistics

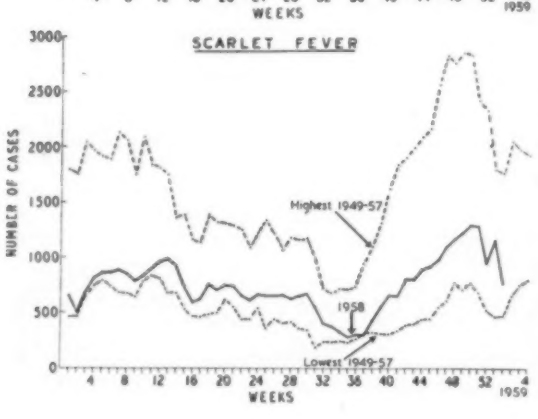
Unusual Infection at Nottingham

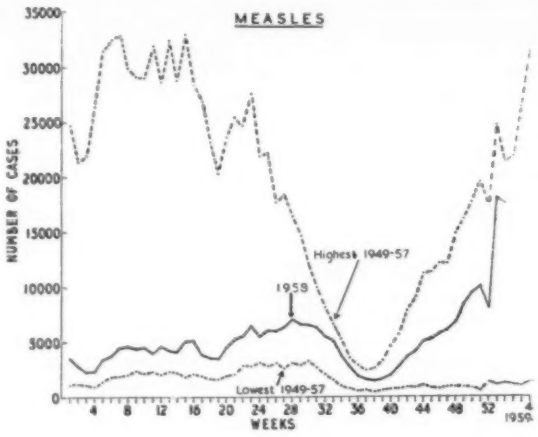
An outbreak of infectious diarrhoea at Nottingham General Hospital, thought at first to be due to *Salmonella paratyphi B*, has proved to be due to *S. limete*. 52 cases have been identified, all mild. Though the hospital was closed for a time, the outbreak is now fully under control and wards are being reopened. It is hoped that they will all be functioning fully in a week to 10 days.

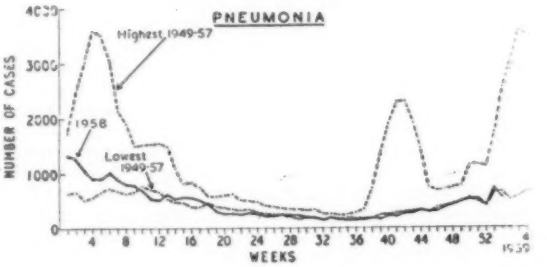
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1949–57 are shown thus ------, the figures for 1958 thus ———. Except for the curves showing notifications in 1958–9, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Week Ending January 10

Large falls in the notifications of infectious diseases, other than acute poliomyelitis, were recorded in England and Wales during the week ending January 10. These included 3,050 for measles, from 18,179 to 15,129, 381 for scarlet fever, from 1,150 to 769, 211 for dysentery, from 886 to 675, 172 for acute pneumonia, from 722 to 550, and 55 for whooping-cough, from 584 to 529.

The largest falls in the number of notifications of measles were 398 in London from 1,466 to 1,068, 313 in Middlesex, from 1,076 to 763, 256 in Lancashire, from 1,830 to 1,574, 252 in Surrey from 804 to 552, 201 in Lincolnshire, from 595 to 394, 187 in Kent, from 719 to 532, and 182 in Wiltshire, from 473 to 291. In contrast to the rest of the country the northern counties recorded an increased incidence of measles, with rises of 96 in Durham, from 537 to 633, 50 in Northumberland, from 101 to 151, and 42 in Cumberland, from 58 to 100. The largest falls in the incidence of scarlet fever were 51 in Lancashire, from 138 to 87, and 49 in Essex, from 107 to 58. Only small fluctuations were recorded in the local returns of whooping-cough. 5 cases of diphtheria were notified, being 1 more than in the preceding week.

The notifications of acute poliomyelitis numbered 43, and these were 3 more for paralytic and 9 more for non-paralytic cases than in the preceding week. The largest returns were Hampshire 26 (Southampton C.B. 14, Winchester M.B. 11), Derbyshire 3, Lancashire 3.

The chief centres for dysentery were Glamorganshire 108 (Cardiff C.B. 59, Rhondda M.B. 40), Yorkshire West Riding 97 (Leeds C.B. 50, Bradford C.B. 12), London 51 (Deptford 9), Surrey 50 (Caterham and Warlingham U.D. 19, Croydon C.B. 13, Coulsdon and Purley U.D. 11), Hampshire 43 (Southampton C.B. 20, New Forest R.D. 18), Lancashire 39 (Liverpool C.B. 14), Lincolnshire 38 (Grimsby C.B. 22, Boston M.B. 10), Essex 35 (West Ham C.B. 10, Walthamstow M.B. 10), Warwickshire 23 (Coventry C.B. 18), Yorkshire East Riding 22 (Kingston upon Hull C.B. 11, Haltemprice U.D. 10), Berkshire 21 (Maidenhead M.B. 15), and Northumberland 20.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **January 3** (No. 53) and corresponding week 1958.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1959					1958				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	4	0	7	0	1	6	1	2	0	3
Dysentery ..	886	71	135	4	5	546	130	68	14	3
Encephalitis, acute	3	0		0		2	0		0	
Enteric fever:										
Typhoid ..	1	0	0	0	1	1	1	0	0	1
Paratyphoid ..	2	0	0	0		8	0	0	0	
Food-poisoning ..	154	27	10	1		137	17	4	0	
Infective enteritis or diarrhoea under 2 years				16	23				6	27
Measles	18,179	1466	58	99	658	3,516	27	91	48	13
Meningococcal infection	25	6	10	2	1	33	3	5	0	
Ophthalmia neonatorum	26	5	2	0		37	3	1	0	
Pneumonia† ..	722	53	265	5	1	1,341	123	386	9	17
Poliomyelitis, acute:										
Paralytic ..	23	3	2	0	4	28	2	0	5	3
Non-paralytic ..	8	1				8	0			
Puerperal fever§ ..	204	41	6	1	1	209	47	4	0	
Scarlet fever ..	1,150	65	83	43	29	651	43	58	21	5
Tuberculosis:										
Respiratory ..	485	64	78	24		481	54	50	12	
Non-respiratory	47	4	8	3		54	4	6	2	
Whooping-cough..	584	11	32	114	75	445	47	24	3	2

DEATHS	1959					1958				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	No comparable figures available.	0	0	0	0
Dysentery ..	0	0		0			0		0	
Encephalitis, acute		0			0		0			0
Enteric fever ..	0	0	0	0			0	0	0	
Infective enteritis or diarrhoea under 2 years	13	0	1	1	2		0	0	0	2
Influenza	21	3	0	0	0		27	3	0	5
Measles		1	0	0	0		0	0	0	0
Meningococcal infection		1	1				0	1		
Pneumonia ..	842	68	27	17			137	41	21	21
Poliomyelitis, acute	6	0		0	0		0		0	0
Scarlet fever ..		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory ..	128	10	10	0	4		11	11	1	10
Non-respiratory		2	0	0	0		1	0	0	0
Whooping-cough..	1	0	0	0	0		0	0	0	0
Deaths 0–1 year ..	392	35	27	9	11		33	31	10	27
Deaths (excluding stillbirths) ..	13,043	1065	731	158	256		1320	702	123	271
LIVE BIRTHS ..	17,361	1512	911	304	415		1385	940	265	317
STILLBIRTHS ..	364	24	21				30	24		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Review of Medical Services.—Sir ARTHUR PORRITT told a press conference on January 14 that the Medical Services Review Committee, of which he is chairman, expects to take two years over its work. Broadly, the first six months will be spent in exploring the field; the second six months in obtaining evidence; the third six months in sorting the evidence; and the fourth six months in preparing the report and recommendations. Of the 36 members of the Committee (see *British Medical Journal*, December 6, 1958, p. 1401) half are under the age of 50. As Sir Arthur put it, "It is a constructive co-ordination of the profession as a whole for the benefit of the patients as a whole." He would not be drawn into naming what he believed were the disadvantages of the medical services at present, but thought it would be unrealistic to say that patients and doctors were quite happy with things as they are. It was the Committee's job to find out why. In doing so, it would bear in mind first and foremost the essential interests of the patient. The ultimate aim was to make recommendations which would lead to an improvement in the health of the people.

X-rays for Miners.—In future every British miner will be entitled to a chest *x*-ray every five years as part of the National Coal Board's campaign against pneumoconiosis. This was stated by Dr. J. M. ROGAN, the board's chief medical officer, at a press conference on January 13. The board has bought nine mobile *x*-ray units each costing £12,800, and will spend £140,000 a year in operating them. It is expected that the pneumoconiosis certification rate will rise sharply in the first few years as previously unsuspected cases come to light, but after that measures to suppress dust should cause the figures to drop to very low levels.

Research on Poliomyelitis.—An electron microscope and an analytical centrifuge, costing £30,000, have been given to the Medical Research Council by the National Fund for Poliomyelitis Research. These instruments will be used in the Council's laboratories at Carshalton for research on tissue cultures as an alternative to fresh monkey kidney in the production of polio vaccine. At present the kidneys of one monkey yield about 1½–2 litres of vaccine. Last week-end newspapers carried reports of the death from gastro-enteritis of over 200 monkeys (about 25%) from a consignment being flown from Ethiopia to Canada for use in the production of polio vaccine. The survivors were treated with streptomycin on their arrival in London.

Infantile Paralysis Fellowship.—The national chairman (the EARL OF SHREWSBURY) and the general secretary of the Infantile Paralysis Fellowship resigned at the Fellowship's annual meeting on January 17. The resignations followed the presentation of the report of a commission of inquiry which Lord Shrewsbury had asked to look into the Fellowship's affairs. The report strongly criticizes the Fellowship's management, and comments on the failure to make the best use of the considerable funds accumulated. More of the money could well be devoted, states the report, to the permanent welfare of polio victims and also, perhaps, to bodies carrying out fundamental research on the disease. The Fellowship, which was founded in 1939, had by 1957 a membership of 14,000, and its total assets are now about £250,000. Its annual income, according to the report, is in the neighbourhood of £100,000. The five-member commission of investigation included two members of the medical profession—the chairman, Mr. T. KEMP HOMER, who is also a barrister, and Mr. A. LAWRENCE ABEL.

French Government Exchange Scholarships.—The Medical Research Council invites applications from British workers in medical science for two scholarships tenable at research institutions in France during the academic year 1959–60. These are offered under the terms of a reciprocal arrangement with the Centre National de la Recherche Scientifique, and are intended for young graduates who have

had some previous experience. Their value is within the range of 50,000–70,000 francs a month, with marriage and travelling allowances. Further information may be obtained from the Secretary, Medical Research Council, 38, Old Queen Street, London, S.W.1. The closing date for applications is March 31.

The Commonwealth Fund.—In the year ended June 30, 1958, this American fund made grants totalling over $3m. (*Annual Report*, 1958). More than 86% of the expenditure was for activities related to the field of health and went chiefly to American universities. However, a few fellowships and awards were made to workers in Britain and in the British Commonwealth. This year up to 30 "undifferentiated" awards will be offered to workers from the United Kingdom. Further details may be obtained from the British Committee of Award, Harkness House, 38, Upper Brook Street, London, W.1.

Rockefeller Benefaction.—In his *Review* of the Rockefeller Foundation's work in 1957, published last month, Dr. DEAN RUSK, the Foundation's president, said that grants that year had totalled over $42m. In 1958 they were $31m., a drop of $11m. In 1957, 532 men and women from 53 countries were holding Rockefeller Foundation awards, of whom 248 received their awards during the year. The holders pursued their advanced training and research in 104 institutions in 20 countries.

Prize for Psycho-analysts.—The Institute of Psycho-analysis offers an annual prize of £20 for an essay on a case investigated by psycho-analytical methods (closing date, May 31). Further details from the Institute, 63, New Cavendish Street, London, W.1.

Oxford University.—Dr. W. M. COWAN and Dr. D. A. T. DICK have been appointed university demonstrators in human anatomy, from January 1 and October 1, 1959, respectively. Dr. R. BRYCE-SMITH has been appointed a clinical lecturer in anaesthetics, from December 1, 1958.

Edinburgh Royal Infirmary.—Professor J. ROMANES, professor of anatomy at Edinburgh, has been appointed chairman of the board of management of the Royal Infirmary.

British Doctors for Australia.—Following its recent recruiting campaign in Britain (*Journal*, October 4, p. 866), the Victoria Hospitals and Charities Commission has appointed 21 British doctors, including three women, to posts in Victorian country hospitals.

Professor Robert Platt, P.R.C.P., is to receive the honorary degree of LL.D. in the graduation ceremonies at Belfast University in July.

Professor K. J. Franklin, F.R.S., formerly professor of physiology at St. Bartholomew's Hospital Medical College, has been elected to an emeritus fellowship of Oriel College, Oxford.

Dr. W. D. Wylie, anaesthetist to St. Thomas's Hospital, London, has left on a six-weeks lecture tour of the Lebanon, Jordan, Iraq, and Iran on behalf of the British Council.

COMING EVENTS

British Association of Allergists.—Annual general meeting January 24, 11 a.m., at the Royal Society of Medicine, London, W.1.

Aids for the Disabled.—Exhibition arranged by the British Red Cross Society, February 18 and 19 (10 a.m.–7 p.m.) at 14 and 15, Grosvenor Crescent, London, S.W.1.

Artificial Limbs and Appliances Centre, Roehampton.—The next course for orthopaedic consultants and senior registrars will be held from March 16 to 20. Details from the Centre, Roehampton House, London, S.W.15.

"The Handicapped Child."—Whole-day symposium arranged by the department of psychological medicine, Liverpool University, March 21. Further details from Dr. J. JARVIE, 77, Bedford Street South, Liverpool, 7.

"Pneumoconiosis."—A symposium arranged by the Chest and Heart Association (formerly N.A.P.T.), April 10 at 3.30 p.m. at the Council Chamber, Council House, Birmingham. Details from the association, Tavistock House North, Tavistock Square, London, W.C.1.

NEW ISSUES

The journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

British Journal of Pharmacology and Chemotherapy.—Issued four times a year (£4 4s. annually). The new issue (Vol. 13, No. 4) includes:

PHARMACOLOGICAL ACTIVITY OF 5-PHENYL-1:3:4-THIADIAZOLE (L 1538), 2-AMINO-5-PHENYL-1:3:4-THIADIAZOLE (L 1460), AND 2-AMINO-5-(2-THIENYL)-1:3:4-THIADIAZOLE (L 1458). G. Maffi and E. Soncin.
THE DISTRIBUTION OF METHYLPENTYNOL AND OF METHYLPENTYNOL CARBAMATE IN TISSUES AND BODY FLUIDS OF CATS. E. Marley and J. R. Vane.
CARDIAC OUTPUT DURING EXCITATION OF CHEMOREFLEXES IN THE CAT. Gwenda R. Barer and E. Nüsser.
THE PHARMACOLOGICAL ACTIONS OF SOME MUREXINE-LIKE SUBSTANCES. V. Erspamer and A. Glässer.
HAEMOGLOBINURIA CAUSED BY PROPYLENE GLYCOL IN SHEEP. B. J. Potter.
THE RELEASE OF ADRENALINE AND NORADRENALINE FROM THE ADRENAL MEDULLA OF THE CAT DURING SPLANCHNIC STIMULATION. N. R. Eade and D. R. Wood.
PROTECTION AGAINST SYSTEMIC POISONING BY MUSTARD GAS, DI(2-CHLOROETHYL) SULPHIDE, BY SODIUM THIOSULPHATE AND THIOCIT IN THE ALBINO RAT. S. Callaway and K. A. Pearce.
THE EFFECT OF SOME OXIMES IN SARIN POISONING. J. P. Rutland.
ANTIVIRAL ACTION OF DERIVATIVES OF ω-AMINOACETOPHENONE. J. Brug, C. A. de Bock, H. D. Moed, and A. J. Klein.
THE UPTAKE OF ADRENALINE AND NORADRENALINE BY BLOOD PLATELETS OF THE PIG. G. V. R. Born, O. Hornykiewicz, and Anne Stafford.
A DEPRESSANT EFFECT OF ACETYLCHOLINE ON THE IDIO-VENTRICULAR PACEMAKER OF THE ISOLATED PERFUSED RABBIT HEART. J. M. Benforado.
THE RELATIVE POTENCIES OF SOME SUBSTITUTED SALICYLIC ACIDS AS METABOLIC STIMULANTS IN THE INTACT RAT. Muriel M. Andrews.
DERIVATIVES OF 3:4-XYLIDINE AND RELATED COMPOUNDS AS INHIBITORS OF INFLUENZA VIRUS: RELATIONSHIPS BETWEEN CHEMICAL STRUCTURE AND BIOLOGICAL ACTIVITY. R. J. Clark, A. Isaacs, and J. Walker.
THE CURATIVE POWER OF 4-(2:6-DIAMINOPYRIMIDIN-4-YLAMINO)PHENYLARSINE OXIDE (COMPOUND 12,065) IN INFECTIONS OF TRYPANOSOMA RHODESIENSE IN LABORATORY ANIMALS. J. R. Baker.
A METHOD FOR RECORDING PERISTALSIS IN ISOLATED INTESTINE. Edith Bülbring, A. Crema, and O. B. Saxby.
OBSERVATIONS CONCERNING THE ACTION OF 5-HYDROXYTRYPTAMINE ON THE PERISTALTIC REFLEX. Edith Bülbring and A. Crema.
CHEMOTHERAPEUTIC SCREENING OF COMPOUNDS AGAINST THEILERIA ANNULATA IN TISSUE CULTURE. F. Hawkins.
THE ACTION OF SYMPATHOMIMETIC AMINES ON HEART RATE IN RELATION TO THE EFFECT OF RESERPINE. D. Bejrablaya, J. H. Burn, and J. M. Walker.
EFFECT OF INHIBITORS OF CHOLINE ACETYLATION ON ACETYLCHOLINE OUTPUT AND MOTILITY IN RESPONSE TO ANTICHOLINESTERASES AND TO DISTENSION OF THE LUMEN OF ISOLATED GUINEA-PIG ILEUM. A. Gioia and C. Morpurgo.
THE DEPRESSOR ACTION OF DOPAMINE AND ADRENALINE. J. H. Burn and M. J. Rand.
THE PERIPHERAL ACTION OF HEXAMETHONIUM AND OF PENTOLINIUM. P. Manteuzzis, Christine Tyler, and Eleanor Zaimis.
EFFECTS OF DRUGS WHICH DEPRESS THE PERIPHERAL NERVOUS SYSTEM ON THE RETICULAR ACTIVATING SYSTEM OF THE CAT. K. A. Exley, Marie C. Fleming, and A. D. Espelien.
A MICROBATH. J. H. Gaddum and R. P. Stephenson.
THE DIFFERENCE IN THE METABOLISM OF INJECTED [^{14}C]HISTAMINE IN MALE AND FEMALE RATS. H. Westling.
THE PHARMACOLOGICAL ACTIONS OF PEMPIDINE AND ITS ETHYL HOMOLOGUE. A. Spinks, E. H. P. Young, J. A. Farrington, and D. Dunlop.
THE NEUROMUSCULAR BLOCKING ACTION OF BENZOQUINONIUM CHLORIDE IN THE CAT AND IN THE HEN. W. C. Bowman.

British Journal of Ophthalmology.—Issued monthly (£4 annually). The new issue (Vol. 43, No. 1) includes:

THE ROYAL OCULIST. P. D. Trevor-Roper.
FUNCTIONAL SPASM OF ACCOMMODATION. L. H. Savin.
PROPTOSIS AS THE FIRST SIGN OF ORBITAL SEPSIS IN THE NEWBORN. E. D. Burnard.
SIGNIFICANCE OF COLOUR CHANGE IN THE CORNEA. J. H. Doggart.
MYECTOMY OF THE INFERIOR OBLIQUE. K. Rubinstein and J. Dixon.
MODIFIED RIDLEY LENSES. E. Epstein.
METABOLISM OF THE DEVELOPING RETINA. I. AEROBIC AND ANAEROBIC GLYCOLYSIS IN THE DEVELOPING RAT RETINA. C. Graymore.
IN VITRO SWELLING OF THE KITTEN RETINA INDUCED BY SODIUM FLUORIDE INHIBITION. C. Graymore.
HAEMORRHAGE INTO THE LENS. P. R. Stevens and S. Chatterjee.
MUCOPOLYSACCHARIDE IN THE SECRETION OF VERNAL CONJUNCTIVITIS—ITS USE AS A DIAGNOSTIC TEST. E. Neumann and N. Blumenkrantz.
ALLERGY TO ANTIVENINE SERUM. S. P. Mathur.
CHIASMAL ARACHNOIDITIS. D. C. Gibbs.
MALIGNANT GLAUCOMA. A. G. Cross.
TWO NEW SURGICAL INSTRUMENTS. R. H. Townsend.

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, January 26

GUY'S HOSPITAL.—5.15 p.m., Endocrine demonstration by Dr. R. I. S. Bayliss: Addison's Disease.

MANCHESTER MEDICAL SOCIETY: (1) SECTION OF ODONTOLOGY.—At Lecture Room, Dental Hospital, 4.30 for 5 p.m., Mr. G. Ashcroft: Extraction of Teeth. (2) SECTION OF GENERAL PRACTICE.—At Large Anatomy Theatre, Manchester University, 8.30 for 9 p.m., Dr. T. R. Malloy: Family Doctor and the Child Psychiatric Service.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. D. Evan Bedford: Pericardial Effusion.

Tuesday, January 27

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor C. V. Harrison: Pathology of Pulmonary Hypertension.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. H. Meara: Eczema in Childhood.

KEIGHLEY AND DISTRICT MEDICAL SOCIETY.—At Skipton General Hospital, 8.30 p.m., clinical meeting.

MANCHESTER MEDICAL SOCIETY.—At Large Anatomy Theatre, Manchester University, 4 for 4.30 p.m., University Lecture on the History of Medicine by Professor R. E. Lane: Miners' Diseases.

ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Colonel N. C. Oswald: Influenzal Pneumonia.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Erasmus Wilson Demonstration by Dr. R. C. B. Pugh: Problems in Bladder Pathology.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Institute Theatre, 5 p.m., Mr. Oswald Lloyd: Pitfalls Associated with Occipito-posterior Presentations.

Wednesday, January 28

BRITISH PSYCHOLOGICAL SOCIETY: MEDICAL SECTION.—At Royal Society of Medicine, 8.45 p.m., Chairman's Address by Dr. A. Plaut: Aspects of Consciousness.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. A. Tickner: Connective Tissue Changes due to Hormones.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. L. Livingstone: Steroid Therapy in Asthma.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. H. G. Hanley: Surgery of Calculous Disease.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—(1) 2 p.m., Professor H. L. Sheehan: Infarction. (2) 6.30 p.m., Professor D. M. Dunlop: Pre- and Post-operative Management of Diabetics and Patients Suffering from other Endocrine Disorders.

ROYAL SOCIETY OF HEALTH.—At Civic Centre, Newport, Mon., 10 a.m., Dr. John Sleigh: Prevention of Four Epidemic Diseases; Mr. R. G. Coslett: The Clean Air Act, 1956—Practice and Problem.

WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At Rembrandt Hotel, Brompton Road, S.W., 7.30 for 8 p.m., dinner meeting. Dr. A. F. Rogers: Trans-Antarctic Expedition.

Thursday, January 29

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. F. B. Byrom: Significance of Hypertensive Encephalopathy.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Professor T. B. Fitzpatrick: Decreased White Pigmentation.

LIVERPOOL MEDICAL INSTITUTION.—Joint meeting with Liverpool Psychiatric Club, 8 p.m.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor J. S. Calnan: Surgical Treatment of Speech Disorders.

ROYAL NORTHERN HOSPITAL.—2.45 p.m., Dr. W. L. Neustatter: Dealing with the Depressed Patient.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. J. Hamilton Paterson: Neurology.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF BIOCHEMISTRY.—At Physiology Theatre, Gower Street, W.C., 5 p.m., public lecture by Professor F. G. Young, F.R.S.: Hormones and Metabolic Processes—(2) Pancreatic Hormones.

Friday, January 30

AIRBORNE MEDICAL SOCIETY.—At Hammersmith Hospital, 6 p.m., clinical meeting.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. G. B. Mitchell-Heggs.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. N. C. Oswald: clinical demonstration.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., clinical lecture by Mr. Anthony Radcliffe. Role of the Sympathetic Nervous System in Diseases of the Ear.

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES.—At 11, Chandos Street, Cavendish Square, W., 7.30 p.m., short papers by Dr. G. Jelinek, Dr. Leach, Dr. Ashworth, and Dr. Eric Dunlop.

PLYMOUTH MEDICAL SOCIETY.—At Royal Naval Hospital, 8.30 p.m., clinical evening.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—(1) 10 a.m., Professor C. F. W. Illingworth: Some Physiological Contributions of the Glasgow School of Surgery. (2) 4 p.m., Dr. J. H. Goodwin: Pulmonary Hypertension.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF PHARMACOLOGY.—At Physiology Theatre, Gower Street, London, W.C., 5.30 p.m., public lecture by Professor W. V. Macfarlane: Chemical Agents and the Slow Potentials of Heart and Muscle Cells.

Sunday, February 1

CAMBRIDGE UNIVERSITY MEDICAL SCHOOL.—2 p.m., symposium on obstetrics and gynaecology.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—10.30 a.m., clinical meeting.

UNIVERSITY COLLEGE HOSPITAL.—10.15 a.m., meet in Front Hall of main Hospital. Lecture-demonstration for general practitioners. Clinical demonstration by Dr. J. F. Stokes: Therapeutic Problems in Liver Disease.

APPOINTMENTS

BIRMINGHAM REGIONAL HOSPITAL BOARD.—D. Tooms, M.B., B.Ch., F.R.C.S., Part-time Consultant Surgeon (seven notional half-days weekly) to the Mid-Worcestershire group of hospitals).

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—R. A. Bruce, B.M., B.Ch., M.R.C.P., Assistant Chest Physician, Cambridge Area Chest Clinic; J. C. S. Leverton, M.D., M.S., M.R.C.O.G., Consultant Obstetrician and Gynaecologist, Peterborough and Stamford Group of Hospitals; F. C. Harris, M.R.C.S., L.R.C.P., D.T.M.&H., D.C.P., Assistant Clinical Pathologist to hospitals in West Suffolk Area; G. L. S. Rankin, M.B., B.Chir., D.Obst.R.C.O.G., Registrar in Obstetrics and Gynaecology, Ipswich and East Suffolk Hospital Group; I. S. Wilson, M.B., B.S., Medical Registrar, West Suffolk General Hospital; N. S. Batheja, M.B., B.S., D.O., Registrar in Ophthalmology, Norfolk and Norwich Hospital; A. P. Carter, M.B., B.S., and Hymie Green, M.B., B.Ch., F.R.C.S., F.R.C.S.Ed., Surgical Registrar, United Norwich Hospitals.

GARRATT, F. N., Ph.D., M.B., Ch.B., D.P.H., Deputy Medical Officer of Health and Deputy Principal School Medical Officer, Wolverhampton.

MANCHESTER REGIONAL HOSPITAL BOARD.—R. S. Miller, M.R.C.S., L.R.C.P., D.M.R.D., Whole-time Consultant Radiologist, Wigan and Leigh Group of Hospitals; R. S. Ferguson, M.D., D.P.M., Consultant Psychiatrist (maximum part-time), Blackpool and Fylde Group of Hospitals and Lancaster Moor Hospital; J. P. Anderson, M.D., M.R.C.P.Ed., D.C.H., Full-time Assistant Physician and Deputy Medical Superintendent at Monsall Hospital, Manchester, with duties at Ladywell Hospital, Salford.

NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD.—J. A. Robertson, M.B., B.S., M.R.C.P., Consultant General Physician, Willesden General Hospital; I. Yentis, M.D., F.F.R., M.R.C.P., Consultant Radiologist, Windsor Group of Hospitals; I. Rosen, M.D., D.P.M., and D. Rumney, M.R.C.S., L.R.C.P., D.P.M., Assistant Psychiatrists (S.H.M.O.s), Portman Clinic; R. A. Gelfer, L.R.C.P.&S.Ed., L.R.F.P.S.Glas., D.P.M., Assistant Psychiatrist (S.H.M.O.), Napsbury Hospital; Jean M. Webster, M.B., B.S., Assistant Pathologist (S.H.M.O.), Ashford Hospital; F. G. Tait, M.B., B.S., D.P.M., Child Psychiatrist (S.H.M.O.), Willesden Child Guidance Centre; Beryl M. Goetzee, M.B., B.S., F.F.A.R.C.S., Consultant Anaesthetist, Highlands General Hospital; S. Benaim, M.R.C.P., D.P.M., Consultant Psychiatrist, Halliwick Hospital; J. N. Aston, M.B., B.S., F.R.C.S., Consultant Orthopaedic Surgeon, Harefield and Northwood Group of Hospitals; D. G. James, M.D., M.R.C.P., Consultant Physician, Royal Northern Hospital; Rosalind I. Bearcroft, M.B., B.S., D.P.M., Assistant Psychiatrist (S.H.M.O.), Hill End Hospital; Dorothy I. Ogden, M.B., B.Ch., Child Psychiatrist (S.H.M.O.), Twickenham and Staines Child Guidance Clinics.

PLEYDELL, M. J., *M.C.*, M.D., D.P.H., County Medical Officer of Health for Oxfordshire, from February 1, 1959.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Castle.—On January 13, 1959, at Bradford, Yorks, to Joan (formerly Ingham), M.B., B.S., and John Castle, M.B., F.R.C.S., a daughter.

Wiley.—On January 12, 1959, at Oxford, to Pamela, wife of A. M. Wiley, M.Ch., F.R.C.S., a daughter.

DEATHS

Aherne.—On January 10, 1959, at 13, Tantallon Place, Edinburgh, Richard John Aherne, *M.C.*, L.R.C.P.&S.I. & L.M., Group Captain, R.A.F. (retired).

Armitage.—On January 9, 1959, at Moorfield, Cumnock, Ayrshire, William Armitage, M.B., Ch.B.

Balck-Foote.—On January 7, 1959, at his home, Culmore Cottage, Fleet, Hants, John Albert Balck-Foote, M.B., Ch.B., D.P.H., Lieutenant-Colonel, R.A.M.C. (retired).

Browne.—On January 9, 1959, James Charles Haines Browne, M.R.C.S., L.R.C.P., of Cunard Building, Liverpool, aged 48.

Cairns.—On January 1, 1959, at his home, Devon House, Whitehall, Bristol, Frederic James Cairns, L.R.C.P.&S.I. & L.M., aged 82.

Caldicott.—On January 16, 1959, at St. Peter's Hospital, Chertsey, Surrey, Charles Holt Caldicott, M.B.E., M.B., Major, R.A.M.C., T.A. (retired), of Strawcock Field, Chobham, Surrey, aged 87.

Chalmers.—On January 11, 1959, at King George V Hospital, Malta, William Ian Chalmers, M.B., Ch.B., of 109, Marina Street, Pieta, Malta, formerly of Edinburgh.

Chesney.—On January 16, 1959, in hospital, George Chesney, O.B.E., M.D., D.P.H., of 39, Pearce Avenue, Parkstone, Dorset.

Clayton.—On January 9, 1959, at West Suffolk General Hospital, Robert Hogg Clayton, M.B., B.S., B.Hy., D.P.H., of 3, Highbury Road, Bury St. Edmunds, Suffolk, aged 53.

Croom.—On January 5, 1959, at 12, Grosvenor Crescent, Edinburgh, David Halliday Croom, M.D., F.R.C.P.Ed.

Erskine-Collins.—On January 7, 1959, James Edward Erskine-Collins, M.R.C.S., L.R.C.P., of Canada House, Watchet, Somerset.

Giles.—On January 3, 1959, Edith Giles, M.R.C.S., L.R.C.P., of 19, Churchill Road, St. Albans, Herts.

Griffiths.—On January 10, 1959, at Kelmscott, Watford, Herts, Thomas Willie Griffiths, M.R.C.S., L.R.C.P.

Hooker.—On January 11, 1959, in hospital, Alfred Wyatt Hooker, M.B., B.S., of Harpenden, Herts, aged 80.

Howe.—On January 5, 1959, George Henry Howe, M.B., Ch.B., aged 82.

Levy.—On January 12, 1959, at 43, Bryanston Court, London, W., Simon Isaac Levy, F.R.C.S., aged 59.

Lewis.—On January 10, 1959, at 149, Altmore Avenue, East Ham, London, E., Carinna Augusta Barry Lewis (formerly O'Neill), M.B., B.S.

McLean.—On January 1, 1959, at Eastbourne, Sussex, Hugh McLean, M.R.C.S., L.R.C.P., D.P.H., of Rosedene, Corsica Road, Seaford, Sussex, aged 79.

Miller.—On January 7, 1959, William Duff Miller, M.B., Ch.B., of 1, Collingham Place, London, S.W.

Mitchell.—On January 7, 1959, in a nursing-home, Eastbourne, Sussex, Alexander Mennie Mitchell, M.B., Ch.B.

Moir.—On January 9, 1959, in a nursing-home, Dundee, William John Moir, M.B., Ch.B., D.P.H., D.T.M.&H., of 15, Victoria Road, West Ferry, Dundee.

Pines.—On January 10, 1959, at his home, 38, Basing Hill, London, N.W., Noe Pines, M.B., D.O., aged 71.

Riddiough.—On January 7, 1959, at 67, Bridge Street, Cambridge, Sidney Riddiough, M.B., F.R.C.S., aged 67.

Stuart.—On January 9, 1959, Richard Stuart, M.R.C.S., L.R.C.P., D.P.H., D.T.M.&H., D.O.M.S., of Barham House, Harrold, Beds.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Intrathecal Penicillin

Q.—*Why is it that penicillin given intrathecally may have a toxic effect ?*

A.—Although penicillin is relatively non-toxic in the usual sense of the term, it is, none the less, an irritant substance, as anyone who has received an intramuscular injection of a concentrated preparation would testify. It is this irritant property of penicillin itself which is responsible for the serious effects that may follow its intrathecal administration. Given intrathecally to animals, it causes convulsions and death. Applied to the exposed human brain at operation, it causes headache, muscle twitching, and cyanosis, and produces marked changes in the electroencephalogram. In view of these serious effects penicillin should be given intrathecally only when its administration by this route is going to be life-saving. The indication is acute meningitis due to a penicillin-sensitive organism, when the drug does not readily pass the blood–brain barrier. The dose should not exceed 10–20,000 units, and the concentration should not be greater than 1,000 units per ml. A free flow of cerebrospinal fluid should be obtained before the drug is injected so that it will diffuse through the subarachnoid space. Larger doses or more concentrated solutions have been followed by the development of adhesive arachnoiditis and transverse myelopathy.

Diagnosis of Diabetes

Q.—*Can a diagnosis of diabetes be ruled out in the absence of glycosuria ? If not, can it be diagnosed by blood-sugar estimations alone ?*

A.—In mild diabetes the fasting urine may not contain glucose, but, unless the renal threshold is considerably raised, sugar will be present after meals in almost all untreated diabetics. Rarely the renal threshold may be sufficiently raised for glycosuria to be absent even when the blood sugar is as high as 250 or even 300 mg.%. If diabetes is suspected, the diagnosis can readily be established by the ordinary glucose tolerance test in the usual way. It should be remembered that the all-important diagnostic feature of diabetes is the raised blood sugar, of which, in the presence of a normal renal threshold, glycosuria is an indication.

Domiciliary Thiopentone Anaesthesia

Q.—*What drugs and equipment should be carried when intravenous thiopentone is given for a dental operation in the patient's home ?*

A.—The following should be carried. (1) *Equipment for the administration of the thiopentone.* Ampoules of thiopentone powder and distilled water, sterile syringes and needles. (2) *Equipment for ventilating the lungs should respiratory depression or arrest occur as a result of overdose.* While oxygen is excellent, air is quite adequate for this purpose. Ventilation is efficiently carried out by means of a face mask and either the Oxford bellows or the Ruben "ambu" bag. A few sizes of rubber airway should be carried. (3) *Drugs for counteracting certain side-effects.* Analeptics like nikethamide or vanillic acid diethylamide may occasionally be useful to stimulate a patient who is a little slow to recover consciousness. A separate box should contain ampoules of papaverine, procaine, tolazoline, saline, and hyalase in case of intra-arterial or extravenous injection.

In addition swabs, mouth gags, and dental props, required for any mouth operation, should also be carried.

Whether and when it is advisable to embark on dental surgery and general anaesthesia in a patient's home is quite another and debatable question. Very good reasons indeed are necessary to justify this practice.

Infecting Rubella

Q.—*Is there any method of infecting a non-pregnant young woman with rubella if prolonged contact with an infected child is not possible ?*

A.—There is no other method available. Serum from patients in the acute stage of rubella has been used experimentally to infect volunteers but not with constant success. Pharyngeal washings from acute cases might be tried, but the results could not be guaranteed. Neither of these methods at the moment is practicable. Although it is a popular idea that girls and young women should be encouraged to contract rubella, the idea is not without its dangers. A young non-pregnant woman is likely to be friendly with young women in the early stages of pregnancy and might easily infect them with rubella.

Decaffeinated Coffees

Q.—*Are decaffeinated coffees completely free of caffeine ?*

A.—Decaffeinated coffees, and coffee extracts, are not completely free from caffeine. By an efficient extraction procedure, however, the manufacturer can remove at least 90% of the caffeine which is originally present in the beans. This degree of extraction at least seems adequate to justify the description "decaffeinated."

Hangover

Q.—*Is there a drug which will alleviate symptoms, in the form of headache, nausea, and sometimes vomiting, in the morning following the ingestion of very moderate amounts of alcohol ?*

A.—People vary greatly in their tolerance to alcohol, but it must be rare for anyone to have serious after-effects from taking what would generally be regarded as "very moderate amounts of alcohol" on social occasions. In such circumstances one would suspect that factors other than the alcohol itself are responsible for the headache, nausea, and vomiting. There is no specific remedy for the symptoms of the "morning after," but an antacid mixture containing sodium bicarbonate and one of the remedies for motion sickness, such as dimenhydrinate or cyclizine hydrochloride, might be tried.

Correction.—Owing to the removal of purchase tax the N.H.S. basic price of 100 "ferroids" is now 6s. 8d., not 8s. 8d. ("To-day's Drugs," January 10, p. 111).

Collected Articles from the "British Medical Journal"

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